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Section of Anæsthetics

President—H. P. FAIRLIE, M.D.

[*May* 4, 1934]

Self-administered Analgesia for the Midwifery of General Practice

By R. J. MINNITT, M.D.

IT has always seemed to me that, until recently, the progress attained in the relief of pain during childbirth came to a standstill with the work of Simpson.

In trying to solve the problem certain main principles have to be considered, which can be briefly stated as follows: (1) The procedure must be simple and inexpensive; (2) there must be no danger to mother or child; (3) labour must not be prolonged; (4) there must be relief from the pains of labour.

This paper will describe a method of analgesia which, I am satisfied, fulfils these conditions. I would mention here that where the word "analgesia" is used it implies insensibility to pain without loss of consciousness.

Gas-and-oxygen has been given for a number of years in obstetric cases, with a large measure of success. This mode of relief, however, could never be made available for all patients.

Although I had been considering the question of gas-and-air analgesia in midwifery, I am indebted to Dr. Howard Jones for the suggestion that this could be used with great advantage in maternity work, and this stimulated me to make the experiment.

After consultation with Mr. A. Charles King, a gas-and-air machine was devised, and no trouble has been spared by him to make the apparatus thoroughly efficient and reliable.

Figs. 1 (p. 34) and 2 (p. 35) show the simplicity of the machine, and details are given of the inexpensive consumption of gas.

The apparatus—an adaptation of the McKesson oxygen-therapy apparatus—consists of a reduced pressure valve, which allows nitrous oxide to be brought down in pressure from the cylinder, so that it can be delivered to a small rubber bag enclosed in a metal drum. An automatic valve prevents the flow of gas when the bag is full. As soon as it deflates through inhalation, more gas is allowed to enter.

The outlet of the machine is divided into two channels, one for the passage of gas and the other for the passage of air, the latter opened at the bottom by a series of small holes round the collar, so that a definite proportion of air is added, making the mixture as constant as possible. Above these channels is a check-valve which intermits the flow, and is only lifted when fresh gas-and-air is inhaled, thereby preventing an escape while the patient exhales. The whole action is controlled by inspiration.

On the face-mask is fitted a spring finger-release, which is pressed down during inhalation, but supplies full air (therefore throwing the machine out of action) should either the analgesia become deep enough to weaken the force used, or at the will of the patient. The expiratory valve is inserted in the facepiece, and is not adjustable, a spring allowing it to rise with expiration.

I desire it to be clearly understood that the apparatus was never intended for the purposes of anæsthesia, so that its use is precluded in the ordinary way for any obstetric operation such as version, the application of forceps, or extensive repair of the perineum.

The machine has been fitted up in two ways, one in a carrying-case as a portable model for domiciliary work (weight about 15 lb. without cylinders), and the other on an aluminium stand for hospital use. I understand the price of each will be the same.

The amount of gas consumed is on the average 35 gal. per hour, which has been

estimated by calculations carefully made in a number of cases. The analysis of the mixture inhaled is approximately 35% nitrous oxide in air.

Technique of administration.—The analgesia is self-administered. The only important point is that the mask must be airtight, and therefore kept in close apposition to the face by the patient.

Scientific work had been conducted to show that by use of the apparatus there is no danger to mother or child.

(*a*) *The mother.* Electrocardiograph tracings of six patients were taken on three separate occasions—the first of these in each case during labour a few minutes before gas-air analgesia commenced. The second electrocardiograph was taken after

FIG. 1.—Portable model.

administration of analgesia for four hours, five hours, and one hour and twenty-five minutes. Analgesia was then continued until delivery in one and a half hours, two hours and thirty-five minutes, and thirty-five minutes respectively. In the last of these three cases the patient was delivered by forceps on account of rigid perineum, but had to be given an open anæsthetic for the repair of the lacerations.

In the other three cases the second electrocardiograph was taken following delivery after gas-air analgesia for two hours and ten minutes, two and a quarter hours, and three and a half hours. The third electrocardiograph was taken a few days after delivery in each of the six cases.

The cardiologist's report states that no change of any significance is produced by the analgesia.

(*b*) *Mother and child.* A table has been drawn up showing estimations of the mother's pulse and fœtal heart rates at approximately equal intervals during gas-air analgesia, which offers good evidence that this has no apparent effect on the rates.

(*c*) *The child.*—Although no ill-effect was observed upon the infant in any of the cases where gas-air analgesia was administered to the mother, sometimes for long periods, it seemed well to carry out a scientific investigation to corroborate this fact.

FIG. 2.—Hospital model.

As a control, blood was taken from a maternal vein and the umbilical cord in a number of patients immediately after delivery, when there had been no administration of analgesia, and the following table of the results was compiled :—

TABLE SHOWING OXYGEN CONTENT OF BLOOD FROM MOTHER AND UMBILICAL CORD IN DELIVERIES WITHOUT ANALGESIA.

Gravida	Duration of second stage		Oxygen content, vols. per cent. (Van Slyke's method)		Condition of child on delivery.
	hrs.	mins.	Mother	Cord	
P.	—	40	10·5	12·9	Normal.
M.	—	20	10·5	12·3	"
M.	—	30	9·5	17·5	"
M.	—	55	14·9	16·8	"
P.	3	45	4·3	9·6	Normal (note length of second stage).
P.	1	45	13·6	13·5	Cord round neck.
M.	—	45	13·25	6·47	Severe asphyxia, cyanosis.
M	—	20	8·2	6·0	Cord round neck, cyanosis.

Inference: Oxygen content of the cord blood is slightly higher than that of the mother when there is no asphyxia of the child.

TABLE SHOWING OXYGEN CONTENT OF BLOOD FROM MOTHER AND UMBILICAL CORD IN DELIVERIES WITH GAS-AIR ANALGESIA.

Gravida	Duration of second stage		Oxygen content, vols. per cent. (Van Slyke's method)		Condition of child on delivery	Condition of mother
	hrs.	mins.	Mother	Cord		
P.	2	15	8·7	13·8	Normal.	Some cyanosis.
P.	1	35	8·8	16·9	,,	,,
P.	1	50	3·6	18·6	,,	Prolonged cyanosis—delivery by forceps.
P.	—	55	10·2	12·4	,,	Some cyanosis.
M.	—	40	10·8	13·5	Cord round neck.	,,
M.	2	30	13·8	10·2	Cord tightly round neck, some asphyxia, cyanosis.	,,
P.	1	10	17·0	8·5	Slightly cyanosed.	No cyanosis.
P.	1	0	17·7	4·9	1st twin 2 lb. 14 oz.	,,
			19·5	6·6	2nd twin 3 lb. 15 oz.	,,

Inference : Oxygen content of the cord blood is much higher than that of the mother when there is no asphyxia of the child.

This shows that when there was no cyanosis or asphyxia of the child on delivery, the oxygen content of the blood from the umbilical cord was slightly higher than that of the mother. In the cases where the child was born showing these symptoms—on account of long delivery, or of the cord encircling the neck—the oxygen content of the blood from the umbilical cord was reduced.

In comparing this table with that of patients having gas-air analgesia, an interesting point is observed. Cyanosis of the mother was rather encouraged, and, indeed, in one case actually produced, in order that delivery could be accomplished by forceps. As one would expect, the oxygen content of the mother's blood was reduced (in this latter case to a very low level), but that of the umbilical cord did not show any significant alteration. With the exception of the cases in which there was some cyanosis of the child, due to obstetric causes, the results of the oxygen content of the blood are much higher than those of the mother.

With regard to the effect of the method on the duration of labour, an average length of the second stage in primigravidæ of under two hours, and in multigravidæ of under one hour, does not warrant criticism on the score of prolongation of labour.

With regard to the most important part of the investigation from the patient's point of view, I leave my audience to judge from the printed reports the value of the relief from the pains of labour attained by this analgesia.

My own impressions are as follows :—

After the administration has commenced an obvious change occurs in the labour ward. In a place previously filled with groans, comparative peace and quiet reign. Vomiting is rare, and fluids can be freely enjoyed. The patient is less tired and worn out by the efforts of labour, through being analgesic, notwithstanding the fact that the natural forces appear to be increased. Amnesia is also produced in most cases, as the following day the mother often states that she remembers nothing about the birth.

The machine was first tried out in two institutions: (1) The Liverpool Maternity Hospital, by Dr. Hilda Garry, a grant having been obtained for this purpose through the kindness of The National Birthday Trust Fund, and (2) The Wellhouse Hospital, Hertfordshire, by Dr. John Elam, under the supervision of H. Roland Segar, the Medical Superintendent. Both of these investigations were conducted under my direction and control. Warm appreciation has been expressed by the Medical Officers in charge of the patients at both these institutions.

The conclusions that can be drawn from the evidence presented cannot, I think, be better expressed than by quoting from the report of the Medical Board of the Liverpool Maternity Hospital :—

"The apparatus is portable and admirably adapted for use in domiciliary work. The method is simple and safe. It *does* relieve pain without interfering with the progress of labour, and without ill-effect on the mother or child."

Discussion.—Mr. L. C. RIVETT said that Dr. Minnitt's apparatus was being tried at Queen Charlotte's Hospital, and that he (Mr. Rivett) had had the detailed reports of 25 cases. In half of these the results had been very good as there had been relief from pain; in the other half the results had not been so good—the patients had actually felt the delivery. There had been premedication with chloral in some cases and with morphia in others, but in no case had any of the basal narcotics been used. The evidence was definite that the second stage of labour was shortened on the average (in fact in only two cases out of the 25 had labour lasted two hours, and in one of those there was a persistent occipito-posterior presentation). He thought that this was due to the relaxation of the soft parts.

Miss F. C. KELLY said that Dr. Minnitt's method of gas-air analgesia had been used at University College Hospital during the past five weeks. In 15 of the 18 recorded cases there was definite relief from pain. There were three failures, two of which occurred in hysterical women who refused to co-operate. The third failure was possibly due to administration for too short a period. It was found that the greatest relief was obtained when the analgesic was given for an hour or longer. One patient had it for fourteen hours, with great relief. It was felt that, at any rate with students, a little chloroform given for the actual crowning and delivery diminished the risk of perineal tears. It could easily be given after the gas-air mixture had been used for the end of the first stage and the greater part of the second.

Dr. LLOYD-WILLIAMS presented a report on the use of Dr. Minnitt's apparatus in 29 obstetrical cases:—

	Number of cases
Primiparæ	
Vertex presentation, spontaneous delivery	19
Breech delivery	3
Twin ,, ...	1
Forceps ,, ...	5
Total	28
Multipara	
Vertex presentation, spontaneous delivery	1
Total	1

Method of procedure.—The following figures represent the sedative administration during the first stage of labour:—

(1) Potassium bromide and chloral hydrate	9
(2) ,, ,, ,, ,, ,, plus opoidine and $MgSO_4$	16
(3) Opoidine and $MgSO_4$	8
(4) No sedative	1
Total	29

In two of the above cases gas-and-air from the Minnitt apparatus was administered at the end of the first stage; in the remaining 27 cases the mixture was given at the beginning of the second stage and continued until the head was crowned in normal cases, or until deeper anæsthesia was required for operative procedure.

In nine of the 20 normal cases, a very satisfactory degree of analgesia resulted from the beginning of the second stage until there was considerable distension of the perineum and the head was almost crowned. Of the remaining 11 normal cases, analgesia was fair in six of these, but poor in five cases.

Twenty normal cases.—Good analgesia in nine cases: fair in six; poor in five.

In one case only was analgesia sufficiently good to allow of extension of the head without causing distress to the patient; this was no doubt owing to the fact that the anæsthetist did not occlude several air-holes as carried out by Dr. Minnitt. The objection to increasing the percentage of gas, by the occlusion of air-holes, was that the patient as a rule became definitely cyanosed.

In 19 cases, gas-and-air was discontinued at the end of the second stage, while chloroform on an open mask was administered to a degree of anæsthesia during the extension of the fœtal head.

Of the nine remaining cases, in three breech deliveries chloroform was administered for bringing down extended legs; four forceps deliveries were carried out under ether anæsthesia; one was a delivery under chloroform; and in the last, a twin delivery, chloroform was used at the end of the second stage for the first infant.

It is evident that in eight of these cases gas-and-air could not be used for the operative procedure necessary to terminate delivery.

In the few cases in which the apparatus had been used, the number of perineal lacerations had not been great. It had been noticed that the head distended the perineum very smoothly during the administration of gas-and-air analgesia, and the transition from gas-and-air analgesia to chloroform anæsthesia was, as a rule, not accompanied by disturbing movements which precipitated a rapid and uncontrolled expulsion of the head, but good control of the head during extension was usually possible.

Remarks.—Dr. Minnitt's apparatus produced a very satisfactory analgesia for use during the first and second stages of labour.

The duration of the second stage was relatively short when gas-air was administered. It was an established fact that gas-and-oxygen administration during the second stage tended to shorten labour.

In no normal case in this series did the condition of the infant at birth give rise to any anxiety.

Perineal lacerations were very few in this series of cases; the steady progress of the head and gradual stretching of the perineum was no doubt an important factor in the evidence of lacerations.

Dr. HILDA GARRY said that in some of the cases morphia had been given a few hours before the gas-and-air analgesia had commenced. Small doses of scopolamine and other drugs had been tried, but little difference had been observed between the cases in which these were employed and those in which they were not.

In most cases the mother did not feel any pain during the delivery, but knew that this had occurred. The condition produced was analgesia—not anæsthesia.

Dame LOUISE MCILROY said that the important point to remember in labour was that the pain was, as a rule, most severe during the latter end of the first stage. Patients did nto complain so much when the cervix had been entirely taken up. For this reason the gas-and-air apparatus would be useful. It was not, however, safe to leave its administration to the patient herself as she occasionally became cyanosed and required supervision.

The gas-and-air apparatus would prove valuable in the hands of midwives who had been trained in its use. Mr. Rivett and herself differed in their views about chloroform capsules. She could see the benefit if half a dozen or so were used, but it was an expensive item when 50 or 60 were employed as sometimes happened. The prolonged administration of chloroform had its dangers, but Mr. Rivett and herself had, at heart, the same aim—that of giving relief from pain to women who were attended by midwives only.

Dr. Minnitt's gas-and-air apparatus seemed to achieve this object with an element of great safety. She (the speaker) thought that sedatives should be given in the first stage of labour in every case. The gas-and-air apparatus would tide the patient over the end of the first stage and the second, and delivery could be accomplished by the chloroform capsules. In this way everyone would be satisfied.

Dr. ARTHUR A. GEMMELL: This method entirely frees the hand of the accoucheur for delivery. The voluntary resistance of the patient in the second stage is largely obliterated. There is, in a high proportion of cases, a definite amnesia of the birth of the child, and, in addition, at the end of labour the mother is much more rested and tranquil than where no analgesia is employed. With the apparatus at its normal setting the healthy mother does not become cyanosed, and a complete breakdown of the apparatus is the only emergency liable to arise.

It is intended that the education of nurses in the use of the method shall shortly begin at the Liverpool Maternity Hospital.

Section for the Study of Disease in Children

President—F. C. PYBUS, M.S.

[*May* 25, 1934]

Congenital Syphilis and Splenic Anæmia in an Infant.—J. C. HAWKSLEY, M.D. (for HUGH THURSFIELD, M.D.).

D. B., female, aged 1 year and 11 months.

History.—Congenital syphilis, treated with "bisoxyl" by Dr. D. Nabarro. The Wassermann reaction became negative. At the age of 1 year and 5 months she was brought up with the history that she was always pale and jaundiced and was underweight. She was admitted to hospital.

Condition on admission (9.11.33).—Small jaundiced infant. Head square-shaped. Abdomen enlarged (see fig. 1, p. 52). Liver palpable three fingerbreadths below costal margin; edge hard, surface uneven. Spleen enlarged; edge four fingerbreadths below costal margin. No free fluid. No other abnormalities in abdomen, heart, lungs, or central nervous system.

Blood-count.—R.B.C. 1,800,000 per c.mm.; Hb. 35% (Haldane); C.I. 0·96; W.B.C. 6,300 per c.mm.; reticulocytes 3·7%; normoblasts 2 per 100 W.B.C. *Differential*: Myeloblasts 1%; myelocytes 1%; polys. 39%; lymphos. 50%; monos. 6%; eosinos. 3%.

Van den Bergh reaction: Indirect positive 1 unit.

Fragility of R.B.C.: Complete hæmolysis in 0·36% sodium chloride solution; trace hæmolysis in 0·48% sodium chloride solution.[1]

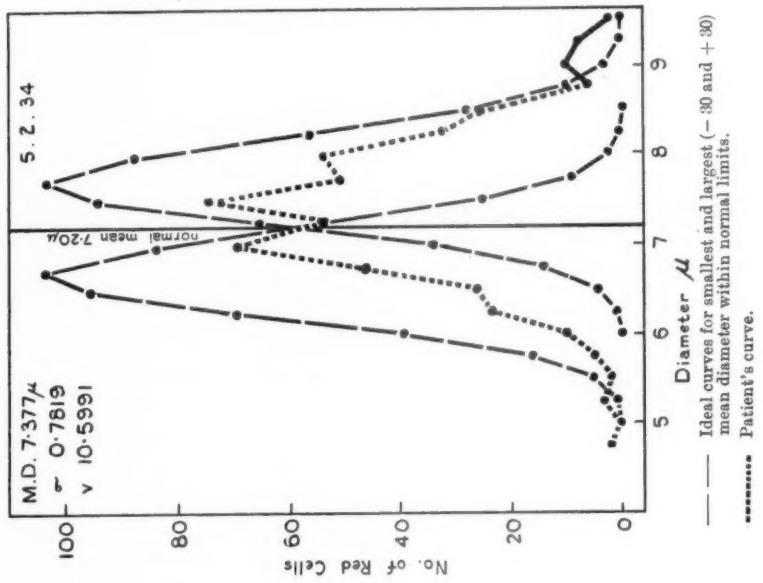
Progress.—Mild pyrexia of irregular type was observed. Transfusions of blood produced only temporary benefit upon her blood-count (a chart of which is given, demonstrating the effects of transfusions, and of splenectomy upon it). Owing to the history of previous syphilis further antisyphilitic treatment was given.

After three months there was no change in the clinical condition, and the blood-count showed only a slight raising of the red cell count and hæmoglobin percentage, attributable to transfusions.

On 14.2.34, following a blood transfusion, the spleen was removed by Mr. O. L. Addison. There was considerable perisplenitis, with adhesions, and the liver was enlarged and coarsely cirrhotic.

Following this there was clinical improvement, and after about five days the temperature became normal, only to rise again once or twice, as the result of a cold or bronchitis. Ascites occurred and was still in evidence on the patient's discharge from hospital five weeks later. It has now subsided.

[1] The van den Bergh and fragility tests were performed by Dr. W. W. Payne.


M.D. 7·377μ
σ 0·7819
v 10·5991
normal mean 7·20μ
5. 2. 34
No. of Red Cells
100
80
60
40
20
0
5
6
7
8
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—— —— Ideal curves for smallest and largest (− 30 and + 30) mean diameter within normal limits.
▪▪▪▪▪▪▪▪▪ Patient's curve.

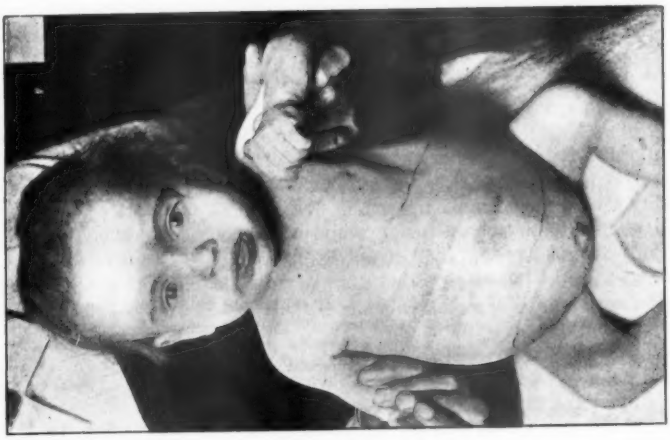
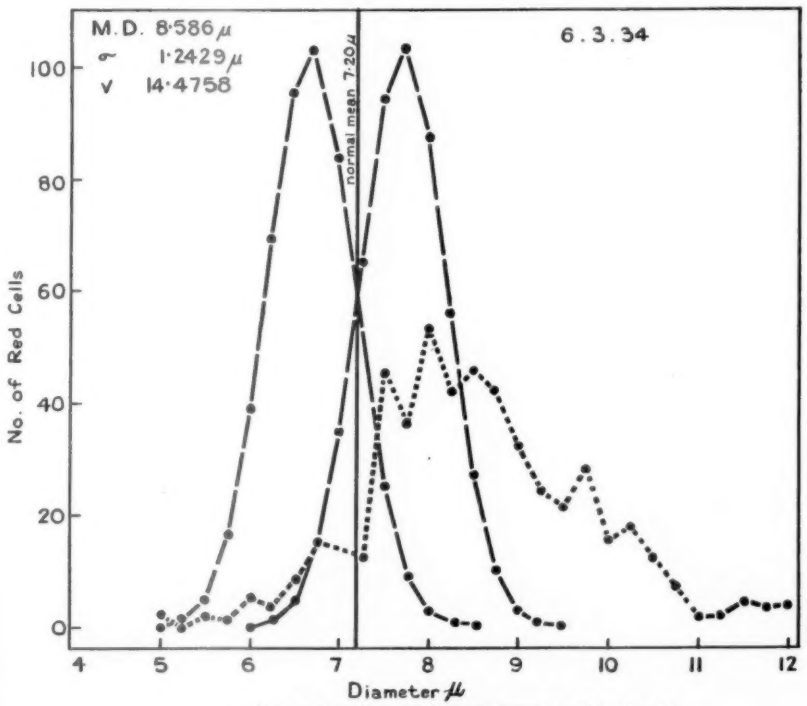


FIG. 1.

The effect on the blood picture was curious. There was a brisk reticulocyte response and an outpouring into the circulation of nucleated red cells, with all varieties of nuclear pattern. In spite of this response the red cell count remained almost unchanged for five weeks ; it is now mounting. Price-Jones curves which, before operation were normocytic, showed megalocytosis and great increase of variability after the splenectomy ; now the mean diameter and variability are moving towards normal (figs. 2, 3, 4). The indirect van den Bergh reaction remained at 1-2 units and the red cell fragility is still raised.

A complete hæmatological chart, giving details, is shown on p. 55.



Summary of pathological report on spleen.—Capsule thickened. Increase in fibrous tissue, particularly round vessels. Germinal centres increased in number.

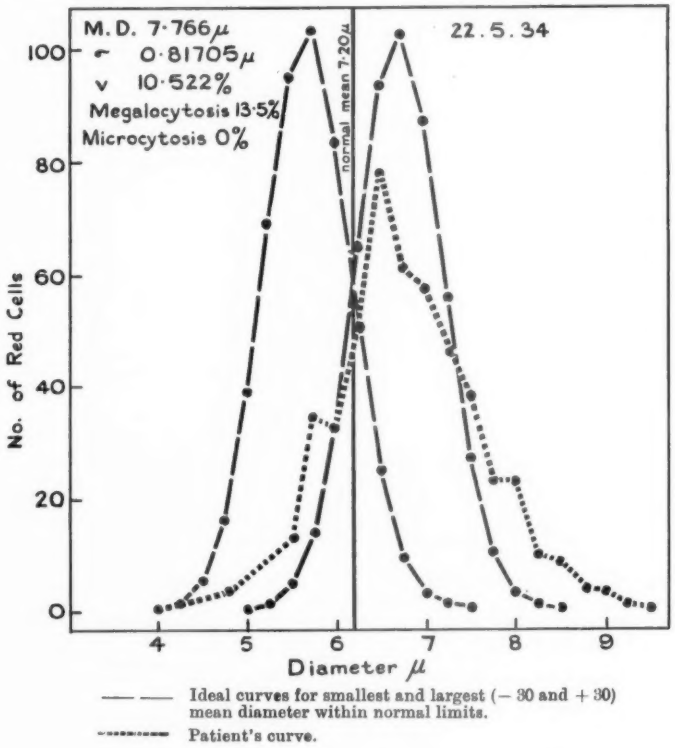
The points of interest are :—

(1) What is the ætiology ? (2) To what type of anæmia is the case most nearly related ? (3) What is the significance of the hæmatological changes following splenectomy ? (4) What is the prognosis ?

In the absence of other evidence of disease, it is probable that the causative factor was congenital syphilis. The clinical and hæmatological picture, before the spleen was removed, was essentially that which is called splenic anæmia, and it must be assumed that, rarely, congenital syphilis can produce this syndrome. The

appearance of the liver and spleen at operation was similar to that in other advanced cases of splenic anæmia and hepatic cirrhosis. As regards splenic histology, Doctor Nabarro reported: "The capsule is thickened, and there is some general increase in fibrous tissue, particularly around the vessels; strands of young fibrous tissue are seen. The germinal centres are enlarged and increased in number, each containing a wide central area consisting of endothelial cells. The vessels of the Malpighian bodies are abnormally large in a few instances. The amount of blood throughout the organ appears within normal limits. There is an increased number of eosinophils."

The erythroblastæmia and megalocytosis which followed the splenectomy are curious phenomena which it will be better to record, but to leave unexplained



until further cases of similar nature are available for comparison. Both these phenomena are known to occur in infants when blood regeneration becomes very marked following severe, and as a rule sudden, anæmias, such as Lederer's anæmia, and, in extreme infancy, erythroblastosis fœtalis. Such a degree of erythroblastæmia, however, is more typical (at this age) of the blood picture associated with von Jaksch's anæmia. Its occurrence after splenectomy in this type of case requires further observation.

The prognosis is probably poor. In spite of definite improvement, the liver is in a cirrhotic state, and the blood-count, though improved, remains subnormal.

Date	Hæmoglobin	Erythrocytes	Reticulocytes % of R.B.C.	Leucocytes	Megaloblasts	Normoblasts	Myeloblasts	Myelocytes	Polymorphs	Lymphocytes	Eosinophils	Mast cells	Monocytes	Remarks
10.11.33	35%	1,800,000	3·5%	6,300	0	2 per 100 W.B.C.	1%	1%	39%	50%	3%	0%	6%	On 21.11.33 received blood transfusion 100 c.c.
23.11.33	45%	2,100,000	4·7%	5,000	0	2 per 100 W.B.C.	2%	0	33%	52%	4%	1%	8%	
1.12.33	40%	2,100,000	1·6%	5,100	2 per 100 W.B.C.	2 per 100 W.B.C.	0	0	41%	50%	2%	0	7%	On 2.12.33 received blood transfusion 100 c.c.
8.12.33	52%	2,800,000	3·7%	6,400	0	0	1%	0	22%	72%	1%	2%	2%	On 6.12.33 received blood transfusion 200 c.c.
14.12.33	50%	3,000,000	4·1%	5,000	0	0	0	2%	35%	53%	0	1%	5%	
21.12.33	50%	2,200,000	3·0%	2,800	0	2 per 100 W.B.C.	0	2%	31%	58%	0	1%	6%	
2.1.34	46%	2,200,000	8·7%	4,300	0	0	0	0	37%	56%	2%	0	4%	
9.1.34	51%	2,100,000	7·9%	9,000	0	1 per 100 W.B.C.	0	1%	51%	46%	0	0	2%	
22.1.34	55%	3,200,000	3·7%	4,700	1 per 100 W.B.C.	2 per 100 W.B.C.	0	2%	36%	58%	2%	0	3%	
31.1.34	45%	2,608,000	2·9%	5,400	0	0	0	1%	38%	54%	0	1%	6%	
5.2.34	42%	2,400,000	3·5%	5,000	0	5 per 100 W.B.C.	0	1%	49%	45%	0	0	5%	
14.2.34	49%	2,400,000	5·8%	4,700	0	2 per 100 W.B.C.	0	0	37%	54%	2%	1%	5%	Transfusion of 200 c.c. followed by splenectomy
15.2.34	51%	2,700,000	5·0%	6,900	1 per 100 W.B.C.	1 per 100 W.B.C.	0	0	56%	36%	0	0	8%	
19.2.34	40%	2,000,000	16·0%	9,000	2 per 100 W.B.C.	89 per 100 W.B.C.	0	2%	31%	50%	1·5%	0	14·5%	
23.2.34	41%	2,060,000	9·3%	18,500	2 per 100 W.B.C.	117 per 100 W.B.C.	0	2·5%	37·5%	49%	2·5%	0	8·5%	
1.3.34	50%	2,300,000	17·0%	9,070	0	56 per 100 W.B.C.	0	0	25%	61%	3%	0	11%	
21.3.34	59%	3,300,000	9·9%	5,500	4 per 100 W.B.C.	32 per 100 W.B.C.	0	2%	18%	61%	8%	1%	10%	
1.5.34	66%	3,500,000	2·3%	15,000	0	3 per 100 W.B.C.	0	0	15%	79%	2%	0	3%	
22.5.34	65%	3,300,000	2·0%	16,600	0	2 per 100 W.B.C.	0	1%	10·5%	83·5%	2·5%	0·5%	2%	

Hæmatological Table: Case of Congenital Syphilis and Splenic Anæmia.

Cooley's Anæmia.—ALAN MONCRIEFF, M.D., and L. E. H. WHITBY, M.D.

The patient, a girl, aged 1½ years, is of pure Greek parentage, born in the Middlesex Hospital. The parents are not related and there is no relevant family history. Pallor was first noted after some feeding difficulties at just under five months of age. An acute abdominal episode then occurred, possibly an intussusception which reduced itself. The infant had been breast-fed for three months, then had "hemolac," then cow's milk with mixed feeding on to a good diet at nine months. After an acute upper respiratory tract infection in April 1934, the pallor became much more evident; the spleen was felt for the first time and the child was admitted to the Middlesex Hospital for investigation.

Clinical summary.—Weight, 19 lb. Moderately well nourished; sixteen teeth, all good. Pale, with pigmentation due to nationality. No bruises, petechiæ, or retinal hæmorrhages. No abnormality of bones found on clinical examination. Heart rapid, with apical systolic murmur. Spleen markedly enlarged but not unduly hard. Liver just palpable. Lymphatic glands not enlarged, except for a few small masses in neck.

Pathological investigations.—Blood-count (10.4.34): Red cells 3,160,000 per c.mm.; white cells 18,600 per c.mm.; hæmoglobin 38%; colour-index 0·5. *Differential* count: Polymorphonuclears 34%; lymphocytes 62%; mononuclears 3%; mast cells 1%; no myelocytes. Anisocytosis, poikylocytosis and polychromasia well marked; normoblasts, 17 per 100 white cells. (On subsequent occasions reticulocyte counts have been made and vary between 3 and 5%. On one occasion a single myelocyte has been seen.)

Fragility of red cells: Slightly increased resistance to saline.

Wassermann reaction negative.

Hæmocrit readings: Vol. index 0·87, saturation index 0·8.

Price-Jones curve shows an average diameter of 7·218 μ, mean deviation 1·22, coefficient of variability 16·9%, megalocytosis 8·6%, and microcytosis 9·6%.

Biochemical investigations.—Van den Bergh reaction: positive indirect with 2·3 units of bilirubin in serum. Urine contained urobilin but no urobilinogen or bilirubin.

X-ray examination.—All the bones show generalized rarefaction, with thinning of the cortex. The metacarpals show a slight degree of trabeculization, but this is not definite in the other bones. The vault of the skull shows some thinning of the tables and the medulla is increased in width. Radiating spiculation is also seen.

Dr. F. PARKES WEBER said that he had been shown familial examples of erythroblastic anæmia ("Cooley's anæmia") in Professor Blackfan's Clinic at Boston. He thought that the present patient (of Mediterranean origin, as were the American cases) was a genuine example of the disease, though as yet the disease was in a relatively mild early stage and there was no family history.

POSTSCRIPT (16.7.34).—The patient has since died. A full account of the pathological details of the case will be given in a future issue of the *Lancet*.

Craniotabes in Four-Months-Old Twins.—K. H. TALLERMAN, M.D.

David and Doris S., now aged 5 months. The twins were aged 4 months when first seen, and were born at full term, weighing 5½ and 5 lb. respectively. They were both entirely breast-fed until 1 month of age, since then each has received four breast feeds and two bottle feeds daily, the feeding being three-hourly, and the artificial food consisting of one teaspoonful of Nestlé's milk in four tablespoonfuls of water. The mother has plenty of breast milk, but her circumstances are such as to make it doubtful whether her diet is satisfactory. The twins have received no cod-liver oil.

The Wassermann reaction of the mother's blood was negative. There is one other

child who is said to be healthy, to have developed normally, and to have been breast fed until 15 months of age.

(1) David S. was sent up to my surgical colleague, Mr. C. E. Shattock, because of "soft and deficient bones of the skull." He was referred to me on 23.4.34.

On examination.—Weight 10 lb. 4 oz. Colour good. Marked craniotabes, with generally very poor ossification of the bones of the vault of the skull. Slight widening of radial epiphyses and prominent costo-chondral junctions. Muscle tone quite good. Skiagram of wrists showed active rickets. Wassermann reaction negative.

R.B.C. 4,300,000 per c.mm.; Hb. 80%; C.I. 0·93 per c.mm.

(2) Doris S. was brought to hospital at my request, no abnormality having been noted, and was examined on 3.5.34.

On examination.—Weight 10 lb. Colour good. Marked craniotabes and slight enlargement of costo-chondral junctions. Muscle tone quite good.

Skiagram of wrists showed evidence of active rickets, less marked, however, than in the case of her brother. Wassermann reaction negative.

R.B.C. 4,450,000 per c.mm.; Hb. 84%; C.I. 0·94 per c.mm.

Neither infant shows any significant abnormality, apart from what is mentioned above.

In view of their condition suitable anti-rachitic treatment has been instituted.

Chronic Intussusception.—F. C. PYBUS, M.S. (*President*).

W. E. T., a boy aged 7, was admitted to a sanatorium in August 1930, with a history that seven weeks previously he had had an attack of abdominal pain, vomiting and diarrhœa. There had been progressive loss of weight since.

On admission to the sanatorium.—There was some suspicion of tuberculosis of the right lung base. The abdomen was full, and the left flank dull on percussion. Free fluid was present, and a mass was found in the upper abdomen extending across the epigastrium under the left costal margin. A diagnosis of tuberculous peritonitis was made.

A week after admission the boy had a further attack of abdominal pain and vomiting, and blood was passed per rectum. The abdominal swelling was still present, but extended further, towards the left iliac fossa. There was no rigidity or tenderness. Examination at later intervals showed free peritoneal fluid, with the mass still extending across the abdomen, which was thought to be infiltrated omentum.

A further and more severe attack of pain, vomiting, and diarrhœa occurred in November 1930. The abdominal tumour was found to have moved into the left iliac fossa and pelvis.

A diagnosis of chronic intestinal obstruction was made, and he was transferred to the Royal Victoria Infirmary, Newcastle-on-Tyne.

On admission.—A sausage-shaped tumour was found in the region of the transverse colon, reaching from the middle line to the splenic flexure. It hardened and softened at times, and the right iliac fossa seemed unduly empty. A diagnosis was made of chronic intussusception of six months' duration.

An attempt was made to obtain characteristic and unmistakable radiographic pictures (figs. 1 and 2).

Operation (December 1930).—The abdomen was opened in the right iliac fossa. The intussusceptum was found to be of the "ileo-cæcal" type and was reduced without much difficulty, the bowel wall being thickened and the peritoneum shaggy. After removal of the appendix the cæcum was anchored in the iliac fossa.

Fourteen months later the boy had been free from any further attacks, and palpation showed the cæcum in its normal position.

I have to thank Dr. Whately Davidson for the radiological investigations.

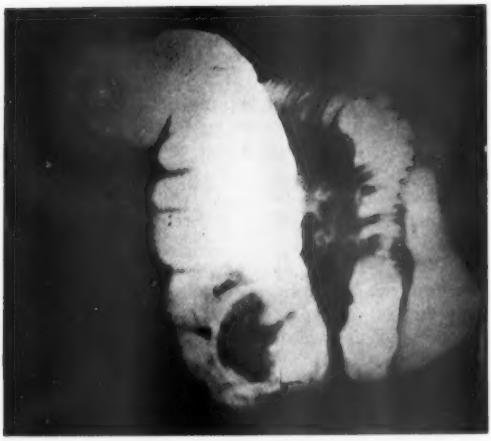


FIG. 1.—A barium enema shows the intussusceptum, the apex in the left iliac fossa. Here the narrow central shadow indicates barium in the ileum and the segmented annular part barium in the colon surrounding the intussusceptum. The apparent filling defect in the right hypochondrium shows barium in the colon at the junction of the sheath and returning layers.

FIG. 2.—Taken after most of the enema had been passed, shows a series of rings due to barium in the colon at the base of the intussusceptum, between the sheath and the returning layer.

Unilateral Post-Operative Chronic Parotitis.—DAVID LEVI, M.S.

The patient, a boy, aged 5 years, is said to have been "healthy" till his tonsils were removed at the Throat Hospital, Fitzroy Square, in 1932. One month after the operation a swelling appeared in the region of the left parotid gland. There have been eight "attacks" since. During the attack the gland swells and is painful, and there is fever. A culture made from saliva taken from Stenson's duct was sterile. Sialography shows dilatations of the terminal ramifications of the duct.

The swelling of the gland subsided, following the distension of the ducts with lipiodol. Up to the present time there has been no recurrence of symptoms and it would appear that the injection of lipiodol has had a favourable influence in arresting the progress of this disease.

Hæmolytic Streptococcal Septicæmia complicating Mastoid Disease. Recovery.—HILDA STOESSIGER, M.D.

The patient, a girl, aged 6 years, was admitted to hospital on April 7, 1934, because of headache and feverishness since the previous night. The right ear had been discharging for one week and had been treated daily in the out-patient department. There was some pain in the left ear on the day before admission. The mother gave no history of previous aural discharge from either ear.

Condition on admission.—The child looked ill and was irritable, and her colour was poor. Temperature 103° F. There was slight tenderness over the tip of the right mastoid process, which disappeared very soon. The ear was discharging freely. The left tympanic membrane was congested. The aural surgeon considered that there was insufficient evidence of mastoiditis to justify immediate operation.

Progress.—High intermittent fever and inconstant signs of meningeal irritation were present. There was a slight shivering attack on April 9. Left paracentesis was performed, with relief of headache and irritability, but no diminution of fever. A white-blood-cell count showed 12,800 cells per c.mm., of which polymorphonuclear cells were 74%. The urine was free from infection.

A rigor occurred on the evening of April 13, and blood was taken for culture. A hæmolytic streptococcus was grown. The cerebrospinal fluid on the 14th was under pressure, but clear. Cells: four lymphocytes and a few red cells; protein, 0·015 grm. %; chlorides, 720 mgm. %.

10 c.c. of polyvalent anti-streptococcal serum were injected intrathecally (the result of the culture not then being known) and 20 c.c. of anti-scarlatinal serum (concentrated) intramuscularly. The latter was repeated again at night and injections were given for the next three days up to a total of 80 c.c. No definite improvement resulted, and rigors occurred again on April 17 and 18.

Bilateral cortical mastoid operations were performed on April 18. On the right side a chronic mastoiditis was found, and there was a bead of pus in the tip of the process. There were a few granulations on the wall of the lateral sinus, but there was no thrombosis or involvement of the dura. On the left side there was some granulation tissue, but no pus, necrosis, or thrombosis. 10 c.c. of anti-scarlatinal serum were given on the evening and morning after operation. The patient made a very rapid recovery, leaving it doubtful whether the serum had been of any value in the treatment.

Familial Hepato-splenomegaly: Two Cases occurring in Brothers.—DONALD BATEMAN, L.R.C.P., M.R.C.S. (for DONALD PATERSON, M.D.).

Henry O'B., aged 4 years, and Terence O'B., aged 2 years.

Complaint (of both boys): "Attacks of yellowness."

Family history.—Parents healthy. Two siblings, girls aged 1 year and 6 years, are both healthy and have never been jaundiced.

(1) Henry: Attack of jaundice associated with cervical adenitis in August 1933. The spleen was two fingerbreadths below the costal margin, and the liver easily palpable. The tonsils had been removed.

April 1934, mild attack of jaundice. The liver and spleen are both palpable. Fragility of R.B.C.: Hæmolysis begins in 0·3% saline; complete in 0·2% saline.

Wassermann reaction negative. Van den Bergh reaction (May 1934) direct and indirect, negative.

(2) Terence: Attack of jaundice at beginning of April 1934. The liver and spleen are both palpable. Fragility of R.B.C.: Hæmolysis begins in 0·35% saline; complete in 0·25% saline.

Blood-count.—R.B.C. 3,208,000 per c.mm.; Hb. 63%; C.I. 1·0; W.B.C. 12,000 per c.mm.; polys. 36%; lymphos. 60%; monos. 2%; basos. 2%.; platelets 250,000 per c.mm.

Van den Bergh reaction: Indirect, well marked positive. In May 1934, direct and indirect, negative. Price-Jones curve: Normal.

Both children made good recoveries from jaundice, but the liver and spleen in each have remained unchanged in size.

Dr. PARKES WEBER thought these cases might be examples of catarrhal jaundice (to which members of some families were apparently specially predisposed), or, more probably, of actual commencing hepatic cirrhosis.

Precocious Puberty in a Boy aged 5.—R. W. B. ELLIS, M.D. (for E. A. COCKAYNE, M.D.).

B. M., male, aged 5 years 4 months. Patient has been well, except for measles during infancy and constant nasal discharge for the past four months. He was brought to hospital in March 1934, on account of being fidgety and difficult to manage. The father was uncertain how long pubic hair had been present, but the boy thought for some months. The patient is of Jewish parentage, and is the younger of two boys (the elder being normal). The mother died following appendicectomy. The boy appears mentally normal for his age, and has not behaved precociously in any way whilst in the ward for two months. He was admitted to hospital on account of precocious puberty, and an intravenous pyelogram was made in order to ascertain if it would give any evidence of an adrenal tumour. It showed the presence of a left-sided hydronephrosis. The boy was operated on (12.4.34) by Mr. O. L. Addison, who removed a large hydronephrosis with stenosis of the ureteropelvic junction, by a left lumbar incision. The left adrenal measured 1½ by 1 in., and was very hard and nodular, feeling exactly like chronic pancreatitis. There was no evidence of neoplasm, and the organ was not removed. The boy made a good recovery.

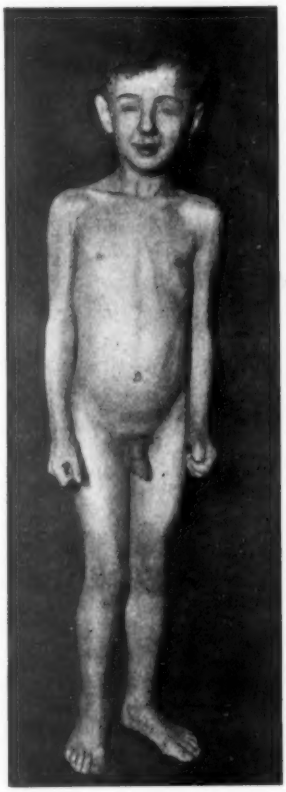
On examination.—A well-developed boy weighing 46 lb., height 47 in. One permanent lower incisor erupting: remainder of first dentition present. Pubic hair of female distribution is present, and the genitalia correspond to those of an adolescent boy of 14 or 15. No other abnormalities found. Prostatic massage produced a bead of prostatic fluid but there have been no emissions or frequent erections. Blood-pressure 100/70. Urine: Nothing abnormal found. Blood-sugar curve normal. Wassermann reaction negative. Skiagram of skull: No evidence of abnormality of pituitary or pineal glands. Long bones: Ossification of a boy of 7. Chest: Thymus not seen.

24.5.34.—The left adrenal gland was removed by the lumbar route, the patient making an uneventful recovery.

The gland when stripped weighed 6·4 grams. It was found that there was a considerable amount of fatty tissue adherent to the gland, which had made it appear firmer and larger at operation than it proved to be after removal. The medulla was brownish-green in colour, and on section showed striking contrast to the paler cortex.

Histological report (Dr. Nabarro): "Microscopically, the zones of the cortex were roughly distinguishable from one another, and it appeared that the lipoid granules of the zona fasiculata might be more numerous than usual. In the particular section examined the medullary layer seemed rather narrower than normal, possibly due to the position of the section. The sections gave a negative fuchsinophile reaction."

Comment.—The patient presented what was apparently an early stage of precocious puberty, the genitalia being those of an adolescent rather than of an adult. There was no abnormality of muscular development, nor did the child show the



Bert M., aged 5 years 4 months, showing small amount of pubic hair and adolescent genitalia.

peculiar facies characteristic of Guthrie's type of precocity; ossification, however, was in advance of the stage normal for the age. The adrenal removed at operation showed no evidence of tumour formation or hyperplasia; unfortunately it had not been possible to examine the right adrenal, as the removal of the left had been carried out by the lumbar route. There was no neurological or radiological evidence of a tumour of the pineal or pituitary glands, and at present the causation of the precocity remains obscure.

Pyloric Stenosis : Adenomyoma of Pylorus.—T. STANLEY RODGERS, M.D. (for A. MAITLAND-JONES, M.D.).

D. W., a girl, aged 10 years, had vomited almost every day since the age of two months. The vomiting was usually projectile, and of late had tended to occur only in the evening. Food taken early in the day has been recognized in the vomited material. The mother had often noticed a prominence of the upper abdomen before the vomiting. She also complained of attacks lasting about a week, in which there was much flatulence and sometimes pain in the left iliac fossa which was relieved by vomiting. The general health had been good throughout and no special dietetic restrictions had been found necessary.

Condition on examination.—A well-developed, well-nourished child. There was a prominence of the epigastrium after meals and well-marked gastric peristalsis was seen, but no tumour could be felt. There were no other abnormal physical signs.

During her ten days in hospital before the operation the child only vomited once; this was a large projectile vomit.

Distal half of stomach removed at operation showing asymmetrical pyloric thickening with resultant obstruction.

Skiagram.—The stomach was greatly dilated and there was considerable delay at the pylorus, but there was no deformity in this area. The duodenal cap filled well and there appeared to be no delay in the duodenum or any dilatation.

Operation (Mr. A. J. Walton, 13.4.34).—A dilated stomach was found, with a hard tumour in the pyloric region. Partial gastrectomy with end-to-side ante-colic anastomosis was performed between the fundus of stomach and a loop of jejunum.

Child discharged three weeks later. Recovery uneventful.

Specimen of stomach.—Smooth, asymmetrical tumour in the region of the pylorus causing obstruction ; histologically shown to be an adenomyoma.

Pathological Report (Professor H. M. Turnbull). *Ectopic Brunner's glands in muscle of Pylorus.*

The specimen removed at operation (S.D. 886, 1934) was a distal segment of the stomach, measuring 8 cm. along the lesser curve and 15 cm. along the greater, with 0·5 cm. of duodenum. The stomach was dilated, and the muscular coat was from 0·2 to 0·3 cm. thick. At the pyloric extremity the muscularis expanded into an asymmetrical thickening. The thickening on the greater curve measured 3 cm. in length and 1·5 cm. in depth, formed

a spindle truncated at the duodenal end, and showed glistening muscle divided into small segments by narrow white lines and by a few white areas. On the lesser curve the thickening was wedge-shaped and only 1·5 cm. long, the base of the wedge facing the lower thickening and measuring 1 cm. It consisted of glistening muscle alone. The lumen between the thickenings was 1·2 cm. long, and closed.

A complete longitudinal section and two transverse sections of the pyloric extremity were examined microscopically. The pyloric thickening is continuous with the circular coat of the muscularis. In its thicker parts it contains many ducts that are lined partly with cells resembling those of the ducts of Brunner's glands and partly with cells suggesting those of Lieberkühn's glands. The ducts are usually surrounded by a mass of Brunner's glands. The glands and ducts are separated from the muscle by a zone of collagenous and elastic tissue, which is sharply defined and usually narrow. A few of the ducts are dilated. There are a few large ducts in the submucosa of the stomach, but not of the duodenum. There are numerous small longitudinal bundles of muscle in the submucosa of the stomach where the thickening of the muscularis is greatest. The ducts and glands show no evidence of progressive growth. Retrogression is shown by a few ducts having lost their epithelium and being surrounded by a broad zone of infiltration with foam cells.

Heterotopia of pancreatic elements in the wall of the stomach is well known, and usually takes the form of yellow plaques of acinar gland tissue in the pyloric region, found by chance at autopsy. Less commonly these thickenings consist of intestinal gland tissue which, by distension of their acini and duct, may give rise to cysts. Matthew Stewart and A. L. Taylor, of Leeds [1], have described four cases of a similar condition in elderly people, giving rise to gastric symptoms, chiefly pain, but with no evidence of pyloric obstruction. In their cases there was evidence of tumour formation—such as active but non-functioning epithelium, with capsules of unstriped muscle surrounding the gland tissue, and signs of compression. In the case here recorded there is no such appearance of neoplasia. The gland tissue seems merely to have wandered to an unusual site and, for some reason, caused a secondary hypertrophy of the muscle there. The fact that this occurred at the pylorus and so led to obstruction seems to be due purely to chance.

The origin of these intestinal heterotopias is obscure. Some, according to Lauche [2] (1924) are acquired conditions resulting from chronic irritation such as that surrounding old ulcers of the stomach, or in the nature of a hyperplastic senile change analogous to adenomyoma of the uterus, others are congenital in origin.

1 STEWART, M. J., and TAYLOR, A. L., "Adenomyoma of Stomach," *Journ. of Path. and Bact.*, 1925, xxviii, 195.

2 LAUCHE, A., "Die Heterotopien der ortsgehorigen Epithels im Bereich des Verdauungskanals," *Virch. Arch.*, 1924, cclii, 39.

Partial Congenital Absence of Sacrum and Coccyx and ? Lower Sacral Roots.—T. STANLEY RODGERS, M.D. (for A. MAITLAND-JONES, M.D.).

L.O., male, aged 2 years and 9 months, has suffered from obstinate constipation and urinary incontinence since birth; laxatives have been used frequently since the age of a few weeks, and recently enemata have been employed to remove hard scybalous masses. The child walks well but recently some weakness in going upstairs has been noticed. There is no history of injury to the spine. Birth weight 7 lb. Walked at 14 months. Septic tonsils removed in February 1934.

Condition on examination.—Pale, flabby child with wasting of the buttocks, automatic bladder and patulous anus with almost complete paralysis of anal sphincters and absence of anal reflex. Knee-jerks present and equal; ankle-jerks absent; plantar reflexes not obtained. Sensations appear normal. The lumbar and first sacral spines can be felt normally, but on rectal examination the coccyx and part of the sacrum cannot be felt, and in their place a smooth, hard rim of tissue can be traced round to the ischial tuberosities. There are no other abnormal signs and no other congenital abnormalities have been found.

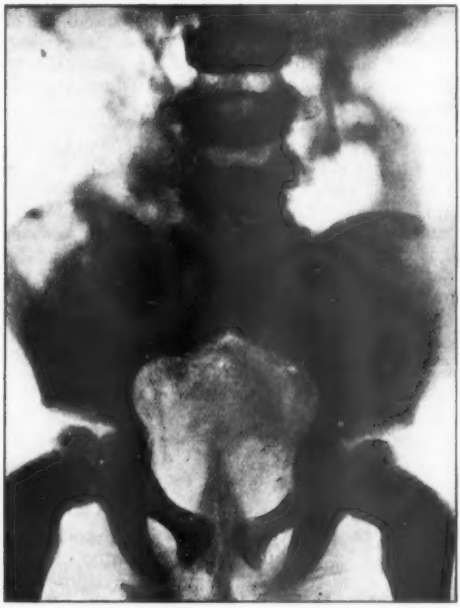


FIG. 1.—Antero-posterior view of spine showing absence of 2nd, 3rd, 4th and 5th sacral segments and of coccyx.

FIG. 2.—Lateral view

Skiagrams.—Absence of coccyx and 3rd, 4th, 5th, and ? 2nd sacral segments. Lumbar spine normal (figs. 1 and 2).

In 1931, H. L. Rocher and G. Roudl of Bordeaux published six such cases and, with 25 collected from the literature, attempted to classify this condition of sacro-coccygeal agenesia. In the first group they put cases of total absence of sacrum and coccyx with gross sphincter disturbances and bilateral club foot. In the second, partial—but considerable—failure of development with sphincter disturbances and sometimes club foot, which symptoms may improve in time. The third group was formed of cases of unilateral failure of development and was occasionally accompanied by nervous symptoms. In the last group were cases of coccygeal aplasia found by chance in skiagrams of this region. It is an interesting coincidence that, despite the rarity of this condition, a similar, though less severe, case without nervous symptoms was seen at the London Hospital a few days after the case here described was diagnosed.

Dr. N. B. CAPON said that he had recently seen a child, aged 1 year and 2 months, who showed symmetrical flaccid weakness, with under-development, of both calves; the knee-jerks were present but the ankle-jerks were absent. No superficial trophic changes were found and anæsthesia could not be demonstrated. The coccyx was absent, but the sacrum seemed to be quite normal.

Healed (Calcified) Miliary Tuberculosis of the Lungs. — J. N. O'REILLY, B.M., M.R.C.P. (for DONALD PATERSON, M.D.).

D. R., a girl, aged 8½ years, attended the Hospital for Sick Children in April 1934. She had had a feverish cold and cough about three weeks previously, and again about three days before the hospital visit.

The previous health had been good, except for pertussis at 2½ years of age, followed by bronchopneumonia. The family history showed that two near relatives had died of pulmonary tuberculosis. The Mantoux reaction was positive. Only a few scattered rhonchi were found on physical examination.

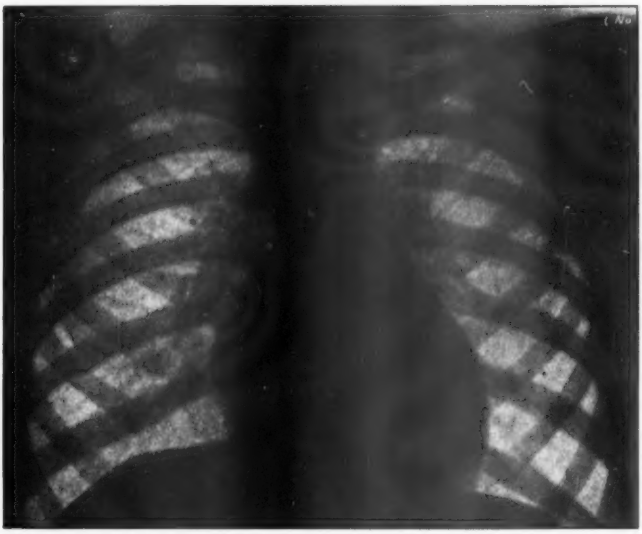
A skiagram shows round calcified foci of various sizes and densities scattered through both lung fields.

The case is one of considerable interest, in that it exhibits what may be regarded as an intermediate form of hæmatogenous spread, between the extremes of the primary focus on the one hand, and miliary tuberculosis of the lungs on the other.

The existence of such forms has long been part of the theoretical teaching on tuberculosis, principally in the German schools. It is supported by many facts, not least of which is the demonstration by Liebermeister [1] of the existence of tuberculous bacillæmia without miliary disease. The spread may take place either in the pulmonary or systemic circulations. In the majority of cases there are no clinical symptoms or radiological appearances. In certain cases, however, when the allergic condition of the patient is suitable, the circulatory spread may give rise to clinical and radiological signs. Clinically, the signs may be no more than cough and vague ill-health. Radiologically, various types of lesion are described. They vary from scattered infiltrations of transient nature, which are often exceedingly difficult to recognize, to cavitating hilar lesions which heal spontaneously. Probably the Assmann focus is no more than one of these forms, conditioned by puberty, external superinfection and, probably, other factors. The present case is, I think, best explained on the grounds that circulating bacilli have settled in the lung tissues, and begun to set up destructive caseous lesions, and then, presumably on account of the arrival of conditions favourable to resistance, have been hemmed in and finally subdued by the patient's rising immunity.

This particular condition is by no means common. I have been unable to trace more than a few cases in the literature. The classical description is by Burkart [2]. He describes the autopsy findings of six such cases, all in adults who had died of

unconnected conditions. Three other cases are described by Edel [3]. Stivelman [4] reports one case, Opie and Anderson [5] five cases, Baer [6] one case, and Blaine [7] three cases.



With regard to prognosis, the condition can only be regarded as stable if the source of the bacilli—that is, the glands of the primary lesion—becomes quiescent. While this focus remains active, it is clear that the blood-spread is held in check or favoured by the condition of the patient's immunity.

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3 Edel, *Beitr. zur Klinik der Tuberk.*, 1932, lxxx, 599.
4 Stivelman, *Am. Rev. Tuber.*, 1932, xxvi, 437.
5 Opie and Anderson, *Am. Rev. Tuber.*, 1920, iv, 629.
6 Baer, *Am. Journ. Dis. Child.*, 1924, xxvii, 110.
7 Blaine, *Am. Journ. Roent.*, 1924, xi, 233.

Mongolian Blue Patches.—J. D. Rolleston, M.D.

The patient is a male infant, aged 1 year and 9 months, the son of a Chinese father and mother. He presents typical Mongolian patches, extending over the back, from the upper dorsal region to the natal cleft inclusive, the buttocks, the antero-external aspect of the left thigh and the back of the upper arms. The child is dark-haired and blue-eyed and presents the typical features of a racial Mongol. The case is presented on account of the unusually extensive distribution of the patches.

[*A report of the cases of* Osteopetrosis ("Marble Bones"; Albers-Schonberg's Disease) in Two Brothers, *shown by Dr. R. W. B. Ellis, will be published in the next issue of the* Proceedings *of the Section.*]

Section of Comparative Medicine

President—R. T. LEIPER, M.D., F.R.S.

[*May* 23, 1934]

DISCUSSION ON CORYNEBACTERIUM INFECTIONS, WITH SPECIAL REFERENCE TO CASEOUS LYMPHADENITIS OF SHEEP

Professor J. B. Buxton.—The best-known species of the genus *Corynebacterium* is no doubt the Klebs-Loeffler bacillus. Of diphtheroids pathogenic for animals, *C. pseudo-tuberculosis ovis*—often referred to as the Preisz-Nocard bacillus, and the cause of caseous lymphadenitis in sheep and of ulcerative lymphangitis in horses—is the best known.

Kitt demonstrated its presence in bronchopneumonia of cattle, Sivori in a similar condition in sheep, Nocard in catarrhal pneumonia of calves, Carré and Bigoteau in *mal rouge* of sheep, while Sérés and Guillaume found the organism in swine, and Lignières in rabbits and guinea-pigs. Bull (1933) recovered it in pure culture from the prescapular lymphatic gland of a cow affected with a granulating wound on the forelimb.

The following definition of *Corynebacterium* is from the M.R.C. Monograph on *Diphtheria*:—

"Gram-positive rod-like forms, arranged usually in a palisade, not acid-fast, often with club-shaped swellings at the poles, generally with irregularly stained segments or granules, non-motile, without endospore formation, growing aerobically or under micro-aerophilic conditions, but often capable of anaerobic cultivation, never forming gas in carbohydrate media, in which they may or may not produce acidity; they may or may not liquefy gelatin or serum."

The Preisz-Nocard bacillus produces acid in glucose and maltose—sometimes in dextrin; on broth a pellicle develops.

The presence of small granules within the organism suggested to Cassamagnaghi (1932) the possibility of obtaining filtrable forms which might be capable of producing infection. He accordingly filtered emulsions of infected glands through Chamberland L_1 and L_2 candles. The filtrates were injected subcutaneously into guinea-pigs, and produced lesions which were in all respects similar to those found after the injection of unfiltered emulsions. The Preisz-Nocard bacillus was recovered in cultures from the glands. From these results the existence of a filtrable form has been suggested.

A soluble toxin is formed which is lethal to guinea-pigs in doses of from 0·1 c.c. to 1·0 c.c. of the filtered culture. The toxin is said to be neutralized to some extent by diphtheria antitoxin, but guinea-pigs immunized to withstand several fatal doses of Preisz-Nocard toxin succumb to a fatal dose of diphtheria toxin (Brocq-Rousseu and Urbain).

Considerable variation is shown in the toxigenic properties of different strains.

The virulence of the strain does not appear to depend upon its toxin-producing power, since strains which are almost incapable of forming toxin in artificial media are nevertheless able to produce extensive lesions when introduced into the body.

Caseous lymphadenitis of sheep.—This disease, which is also known as pseudo-tuberculosis, is a chronic affection, occurring sporadically or as an enzootic. It is characterized by the formation of caseous lesions, especially in the lymph-glands, and in some cases by pronounced wasting and cachexia. It has sometimes been observed in an epizoötic form.

The disease has been reported from time to time in most European countries and is said to be common in parts of North America. It is of considerable economic importance in parts of Australia and South America. It is sometimes said to have been observed in this country, but experimentally it seems that British breeds of sheep are relatively susceptible to infection and, from observations which I made a few years ago, the disease would appear to be transmitted readily under natural conditions in England. It is reasonable therefore to assume that, if the disease did exist in this country, a considerable proportion of the sheep would be affected, and, of course, that is not so.

If the lesions are confined to the internal organs, the presence of the disease is frequently not discovered until the animal is slaughtered, or it may show indefinite symptoms of a slowly progressive anæmia or cachexia. In many instances it may be recognized during life by the presence of painless swellings or "tumours," usually in the prescapular and precrural regions. In such cases the general health may not be affected unless the enlarged glands interfere with locomotion. Such "tumours" when present in breeding stock are usually removed by shepherds.

Infection of the lungs gives rise to symptoms of a chronic bronchopneumonia with a painful cough and muco-purulent nasal discharge. There is frequently a muco-purulent discharge from the eyes, and usually some wasting, even with animals in which the lesions are confined to the lymphatic glands.

The lesions.—In the early stages the lymph-glands are watery or gelatinous in appearance and contain a varying number of small circumscribed nodules enclosing caseous pus. In more advanced cases the whole gland may become transformed into a caseous mass. The pus varies in colour from yellow to green and in older lesions shows on section a laminated appearance, like that of an onion, the periphery of the lesion being composed of a thick wall of connective tissue with a smooth inner surface. The lung lesions vary from small greenish nodules to tumours the size of a goose egg with a structure similar to that of the gland lesions. Subsequently, lime salts may be deposited giving the caseous mass a mortar-like consistency and a greyish colour.

Pathogenicity.—In sheep the subcutaneous inoculation of artificial cultures may result in a local abscess or may be followed by extensive enlargement of the regional lymphatic glands and the development of foci in the lungs. Sometimes the local changes are more acute and consist of extensive œdema. Intravenous injection of from approximately 250,000 to one million organisms is followed by the development of lesions throughout the body (Buxton, 1930). When organisms are given by the mouth in doses of approximately ten million, lesions are found principally in the lungs, while in the abdominal organs the mesenteric glands alone may contain a few foci. The submaxillary, pharyngeal, and bronchial glands appear to be the most extensively infected, while the superior cervical and mediastinal are involved to a much smaller extent. When the infecting dose is administered through a stomach-tube so that contamination of the buccal cavity may be reduced to a minimum, the submaxillary, pharyngeal, or bronchial glands appear to be almost always affected and usually the lungs also (Buxton, 1930).

Seddon (1929) and Carne (1932), however, found it difficult to infect sheep *per os* with cultures or pus, while Carne and Ross (1932), found that infection by this

route was not facilitated by injuries due to wandering parasites such as *Œsophagostomum columbianum*.

Young lambs appear to be readily infected by applying very small amounts of culture to the scrotum after castration or to the stump of the tail after amputation. Healing of such wounds is delayed. Lesions also occur in the lungs and various lymphatic glands and, to a smaller extent, in the liver.

Bull (1933) found that lambs showed a considerable degree of resistance to subcutaneous injections of cultures and to pus applied to wounds even in mixed infections or together with sterile dust.

In guinea-pigs, after subcutaneous inoculation there is a local caseous nodule, the lesion as a rule subsequently extending to neighbouring lymph-glands or internal organs. In male guinea-pigs, after intraperitoneal inoculation, the enveloping membrane of the testes becomes covered with a purulent fibrinous exudate, but the reaction is usually less severe than that produced by *Pf. mallei*.

The natural method of infection is not yet known definitely.

Woodruff and Gregory (1929), Seddon (1929), and Seddon, Belschner, Rose and Blumer (1929) concluded that the most usual method was by the contamination of wounds during shearing, while Seddon and Belschner (1933) considered that wounds were more likely to become infected in the counting-out pens and yards rather than during shearing. The droppings of infected animals would seem to be a likely means of spreading the infection. Carré found large numbers of the organism in the droppings of apparently healthy animals, while Bull (1933) recovered the organism with comparative ease from the soil of the camping grounds of sheep on a property where the disease was enzootic. Murnane (1933) endeavoured to infect guinea-pigs by contaminating wounds with sweepings of counting-out pens of a shearing shed. He used 127 guinea-pigs, of which 34 died from septic infection, but none of the remainder, killed six weeks later, showed infection with the Preisz-Nocard bacillus. A negative result was also obtained in the case of 24 guinea-pigs with wounds contaminated by dust from sheep camps on affected properties.

The question whether the bacilli can lead a saprophytic existence under favourable conditions on such sites has not been determined, so far as I am aware. Buxton (1930) found that eight out of ten sheep which had been in contact with experimental animals, two of which were discharging pus from abscesses, became infected. From the nature and distribution of the lesions there was reason to suppose that the part primarily infected was the thin skin covering the udder and sternum and that the organisms might have been transmitted by biting insects.

Diagnosis.—Following the observation of Vallée and Bossavy that extracts of cultures of the Preisz-Nocard bacillus provoked a local reaction when inoculated under the skin of the eyelid of horses affected with ulcerative lymphangitis, Carré (1923) employed a similar method in sheep. The dose of toxin (0·25 c.c.), injected into the conjunctival tissue of the eyelid, provoked in infected sheep, usually about 12 hours later, a more or less pronounced swelling which was always appreciable when compared with the other eyelid.

Descazeaux (1930) prepared a similar diagnostic agent from virulent strains of the organism grown in Martin's broth for twenty-four hours. The cultures were filtered through Chamberland F.5. filters. Injections into the skin or caudal fold in naturally or experimentally infected animals produced after twenty-four hours swelling, heat and redness which persisted for from twelve to twenty-four hours.

Césari (1930) and Cassamagnaghi (1931) used a similar filtrate obtained from old broth cultures; Césari referred to this reagent as "preisz-nocardine." Favourable results were claimed in sensitized guinea-pigs and in sheep.

More recently, Carne (1932) carried out tests with material prepared after the fashion of tuberculin, using cultures several weeks old. He was unable to confirm the results of previous workers and concluded that "all the allergic reagents so far tested failed to show a degree of efficacy which would render them of value for the accurate detection of infected animals."

Protective inoculation.—Carré (1933) attempted to vaccinate lambs by giving subcutaneously two vaccines of increasing strength (strength not stated), the first a few hours after birth and the second fifteen days later. It was found to be ineffectual in preventing the

suppurative lesions but the more or less acute toxic forms of the disease were said to be prevented.

Brocq-Rousseu and Urbain (1925) attempted to vaccinate guinea-pigs by means of *anatoxin*. They found that the maximum toxin content was obtained in Martin's broth after seven to ten days at 37° C., guinea-pigs of 600 gr. being killed in from twelve to twenty-four hours by doses of from 0·1 c.c. to 1·0 c.c. The culture was filtered through L3 candles and treated with formalin (three parts per 1,000) and incubated. A non-formalinized toxin was used as a control. After four days the formalinized toxin failed to kill guinea-pigs in doses of 5 c.c. while the non-formalinized killed at 4 c.c. After eight days this also became inactive. After one month in the incubator their antigenic properties were tested in guinea-pigs. The modified toxins were found to protect guinea-pigs of 600 grm. against three to five fatal doses of toxin when given in two doses of 3 c.c. with an interval of twenty days. Doses of 1 c.c. did not afford any protection. The vaccine was specific, for all the guinea-pigs which survived the test-dose were subsequently killed by a fatal dose of diphtheria toxin.

The Bacteriological Laboratory, Laigle, prepares a vaccine consisting of a saline suspension of 4,000 million organisms per c.c. The dose is 1 c.c. and one dose only is given.

Experiments carried out by myself with a similar vaccine did not prove successful. The vaccine consisted of a formalinized saline suspension of 25,000 million organisms per c.c. The immunizing effect of one or two doses of 5 c.c. and 10 c.c. respectively with an interval of two or four weeks was tested, from one to three months later by the intravenous or oral administration of culture or pus. Vaccinated sheep and lambs were only slightly less infected than the control animals when killed three months after the test dose. Local caseating lesions were produced by the vaccine in a number of the animals but there was no evidence of extension to neighbouring lymph-glands or other areas of the body.

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Dr. H. R. Carne said that knowledge of the bacteria classed as members of the genus *Corynebacterium* was at present incomplete. Although, apart from the type species *C. diphtheriæ*, the validity of a limited number of species had been generally accepted, much confusion existed concerning the rest, and further, the relation of known species to one another had received little attention. Of the numerous species described, five only had been clearly recognized as pathogenic, viz. *C. diphtheriæ*, *C. ovis*, *C. pyogenes*, *C. equi* and *C. pseudotuberculosis murium*, and to these had recently been added a group of organisms isolated from the human pharynx, which appeared to possess properties intermediate between those of *C. diphtheriæ* and *C. ovis*.

C. ovis and *C. pyogenes* were well known to veterinary bacteriologists as causing common suppurative conditions in animals. There was much confusion in the literature between these two organisms, partly due to their similar morphology, and to the similarity in the characters of their lesions, and partly to the fact that both cause natural infections in sheep.

In a detailed bacteriological examination of about sixty strains of *C. ovis*, isolated from lesions in Australian sheep, all the strains showed some liquefaction of gelatin

when grown on slopes at room temperature; acid was produced by all strains in dextrose, lævulose, galactose, glycerine and maltose (in the latter all but three), whereas raffinose, arabinose, inulin and salicin were not attacked; the action on saccharose, lactose, mannite and dulcite was variable. No indol was produced, the Voges-Proskauer reaction was negative, four strains showed nitrate reduction, and thirty-six produced hydrogen sulphide.

Certain strains formed a hæmolysin capable of causing intravascular hæmolysis and icterus in sheep after intravenous inoculation of culture, though these signs had not been observed in the natural disease in sheep in Australia. Hæmolysis could also be demonstrated *in vitro* in the depths of blood-agar plates, but was inhibited by the presence of free oxygen if plates were sown on the surface. Cells of different species differed in their sensitivity to the hæmolysin, sensitivity decreasing in the following order: guinea-pig, rabbit, horse, sheep. The hæmolysin appeared to be closely linked with the bacterial cell and could not be separated from it. It was thermolabile, non-antigenic, and apparently unrelated to exotoxin or to virulence. The capacity to produce hæmolysin did not appear to be fixed, some strains being non-hæmolytic, others hæmolytic, and there was a tendency for mixed types of colonies to develop in subcultures from single colonies.

C. ovis remained alive for long periods in caseo-purulent material from natural lesions, often even when desiccated. It was readily destroyed by heat and direct sunlight. Vitality was unaffected after long periods of refrigeration. The washed bacteria are readily destroyed by common disinfectants, but bacteria embedded in caseous material were much more resistant unless a fat solvent was used as a vehicle.

Each of some 200 strains examined produced a typical soluble toxin, and though atoxic strains have been described in the literature, such have not been met with in Australia. Optimum toxin-production had been obtained in a peptic digest of ox-flesh and liver, the toxin having a minimal lethal dose for guinea-pigs of 250 grm. varying from 0·1 to 0·005 c.c. Cultures in this medium passed through siliceous filters gave toxic filtrates, though not without some loss of activity, and the toxin could be concentrated by salting out with ammonium sulphate. Such concentrated toxin, when dialysed free of ammonium sulphate had been dried *in vacuo* and when stored in an atmosphere of nitrogen had retained its activity for long periods. A sample of dried toxin having a minimal lethal dose for the guinea-pig of 0·00008 grm. was taken as a standard for comparative purposes, and a corresponding standard antitoxin was prepared in the horse.

The guinea-pig, rabbit, sheep, goat, pig, horse, ox, dog, and cat were all susceptible to the action of the toxin. The lesion following subcutaneous inoculation in the guinea-pig took the form of an extensive, gelatinous œdema of the subcutis resembling that produced by *B. anthracis*; there were hæmorrhages at the site of inoculation, extensive and often intense subserous and submucous hæmorrhages along the alimentary canal, and congestion of the visceral organs. The adrenals were unchanged.

Intracutaneous inoculation in the guinea-pig produced a marked hæmorrhagic necrosis and infiltration of the skin when large doses were employed, but small doses produced a reaction resembling that produced by diphtheria toxin except that it was more papular and more transient.

Washed bacterial bodies, which had been heated to 60° C., were lethal for guinea-pigs after intraperitonal inoculation of 0·05 grm. This somatic toxic action was independent of that of the soluble toxin, and the agent responsible was heat-stable and pyogenic and appeared to be non-antigenic.

The lesions produced by *C. ovis* took the form of chronic abscesses, there being no evidence of acute or chronic intoxication, though the serum of infected animals contained considerable amounts of specific antitoxin.

Natural infection by *C. ovis* occurred in the sheep, the goat and the horse, and

occasionally in the ox. In the horse the disease took the form of an ulcerative cellulitis. The incidence of this disease apparently only assumed considerable proportions when horses were kept under certain war conditions. It had never been observed in Australia where infection of the sheep was common.

Infected animals developed specific agglutinins and sensitizers, and also showed specific hypersensitivity to substances contained in old cultures. Immunological reactions based on these specific responses to infection had not proved to be sufficiently accurate for the purposes of diagnosis, though experiments in progress indicated that a test modelled on the Schick test might prove of value.

Antitoxic immunity, either active or passive, conferred no protection against infection. Serial inoculations with vaccine of killed organisms had also failed to confer any significant protection of guinea-pigs and rabbits against infection, but encouraging results had been obtained with small groups of sheep, and experiments in the field were being extended.

With regard to the epizootiology of caseous lymphadenitis of sheep: The disease was widely distributed throughout the world and occurred in all the principal sheep-raising countries, with the exception apparently of Great Britain. In Australia, the incidence of infected flocks varied greatly. There was some evidence that English breeds of sheep were more susceptible than the merino. Incidence increased with age, and animals which had been shorn showed a higher incidence than unshorn animals. Sex appeared to have little influence on incidence.

Post-mortem examination on over 1,000 infected sheep of various ages and both sexes showed that the greatest incidence of lesions was in superficial lymph-glands, indicating that the infection entered from the surface of the body. The available evidence indicated that the common portal of entry of the causal organism was through wounds. In young animals lesions were almost exclusively in superficial lymph-glands, but as age advanced, metastatic lesions developed in deeper lymph-glands and in the lungs, and in a small proportion of old animals in the liver, spleen, kidneys, etc. Primary lesions in abdominal organs were very rarely found, if at all.

Lesions in lymph-glands tended to persist, though a number might rupture and heal completely, or undergo retrogressive changes with final disappearance of the causal organism.

Considerable attention had been paid to natural methods of infection. At first it had been considered that the common method was by contamination of wounds with material from superficial abscesses ruptured during shearing, etc. The observations of Bull and Dickinson in South Australia had recently shown that *C. ovis* was capable of leading a purely saprophytic existence in soil and fæces in which it would live and multiply under suitable conditions of moisture and protection from direct sunlight. These observers had also shown the value of the guinea-pig in detecting small numbers of *C. ovis* in contaminated material where cultural methods of isolation had failed. The presence of *C. ovis* in the fæces of sheep had also been reported. In view of these recent findings it might become necessary to modify our earlier conceptions of the common method of infection in sheep.

Dr. G. F. Petrie remarked that Dr. McClean and he had supplemented Dr. M. M. Barratt's observations on the diphtheroid group in some work which they had done on the toxin-antitoxin relations of her human strains, Mair's strain, and *C. ovis*. In their experimental work they were especially concerned with the relation existing between the toxins of *C. ovis* and *C. diphtheriæ*, and they carried out cross-immunity tests with the corresponding antitoxins. As was well known, there was conflicting evidence in published work on the subject of this relationship. Their own observations showed no relation between the toxins and antitoxins of *C. ovis* and *C. diphtheriæ*.

He would mention a few points, without going into details. First, there was the difference in the character of the lesions produced in the skin of the guinea-pig and the rabbit by *C. ovis* toxin and by diphtheria toxin. In the guinea-pig, instead of the flat Schick reaction resulting from the injection of diphtheria toxin, *C. ovis* toxin produced a papular reaction which often gave rise to abscess formation. They had found that the intracutaneous lesions from *C. ovis* toxin in the rabbit were relatively much more severe than those in the guinea-pig and were produced by smaller doses. The lesions were swollen, hæmorrhagic, œdematous, and necrotic, and were obviously quite unlike those caused by diphtheria toxin in the skin of the rabbit.

The experiments of some careful observers indicated that diphtheria antitoxin had a slight degree of neutralizing action on *C. ovis* toxin. He (Dr. Petrie) and his colleague believed that the explanation was to be found in the existence of normal *C. ovis* antitoxin in the serum of some horses. They carried out neutralization experiments in the skin of the rabbit with different horse sera and noted varying degrees of neutralizing activity in the samples. They then prepared a quantity of diphtheria antitoxin by immunizing a group of guinea-pigs with diphtheria toxoid, with the result that the pooled serum had no neutralizing action on *C. ovis* toxin when tested intracutaneously in rabbits. Concentrated therapeutic sera of whatever kind possessed a greater neutralizing action on *C. ovis* toxin than the original natural serum from which they were prepared. This result was what one would expect if the natural antitoxin, like normal diphtheria antitoxin, were present in the pseudo-globulin fraction of the serum. They estimated the titre of normal diphtheria antitoxin in the serum of the same group of horses and ascertained that there was no correlation between the content of normal *C. ovis* antitoxin and that of normal diphtheria antitoxin.

Two horses were immunized with *C. ovis* toxin and bacilli, and cross-immunity tests with their sera were carried out by employing the guinea-pig and the rabbit as the experimental animal, but they were unable to detect any evidence of cross-protection.

They also immunized groups of guinea-pigs with diphtheria and *C. ovis* toxoid, and found no cross-immunity. For example, a guinea-pig withstood 17,000 M.L.D. of diphtheria toxin but succumbed a few days later to less than 2 M.L.D. of *C. ovis* toxin.

Their work as a whole justified the conclusion that the toxins of *C. ovis* and *C. diphtheriæ* were unrelated.

Dr. M. M. Barratt said that, as a medical bacteriologist, her interest in caseous lymphadenitis had been in the causal organism rather than in the disease itself. The points of resemblance and difference between *C. ovis* and *C. diphtheriæ* had always intrigued both medical and veterinary workers. In recent years the interest in the relationship between the two organisms had been stimulated by the isolation from the human nasopharynx of certain corynebacteria which resembled *C. ovis* more closely than typical strains of *C. diphtheriæ* do. (Gilbert and Stewart, 1927 and 1929 [1, 2] ; Mair, 1928 [3] ; Barratt, 1933 [4] .) During the last twelve months Dr. Storer of Nottingham had sent her two additional strains ; Dr. Garrod, St. Bartholomew's Hospital, had sent one, and three had been isolated at the Lister Institute, making eleven strains in all in this country.

Morphologically in young cultures (seven hours or less) these strains might resemble typical *C. diphtheriæ* but in older cultures, even in eighteen hours there was a marked tendency for short and even coccal forms to predominate. Culturally the growth on agar was much thicker than that of typical *C. diphtheriæ*, even thicker than that of *C. ovis*; biochemically the most striking difference from *C. diphtheriæ* was the liquefaction of gelatin.

When inoculated intradermally, as in the ordinary routine virulence test for *C. diphtheriæ*, all the strains in the group produced lesions not only in the unprotected guinea-pig but in that protected by diphtheria antitoxin. This difference from *C. diphtheriæ* in pathogenic effect was confirmed in experiments using the subcutaneous route. Varying doses of 48-hour broth cultures were given with and without a dose of diphtheria antitoxin sufficient to completely protect against at least 45 M.L.D. of a broth culture of a typical strain. In the first five strains studied by her [4] this amount of antitoxin saved the life of the animal when two M.L.D. of Mair's strain were given, or one M.L.D. of another strain (Quitman), but gave no protection at all against even one M.L.D. of two other strains (Stead and Revell). In the case of the fifth strain, it might or might not save the life of the animal if only one M.L.D. were given. A preliminary examination of the six additional strains had shown, however, that the 500 units of antitoxin given might be more effective in saving the life of the animal than was suggested in the earlier series. In the experiments made with five of these, the life of the animal was saved when as much as 5 to 20 M.L.D. were given and probably in the case of the lower values the limits of protection were not reached in the experiments so far made. With the sixth new strain—that sent from St. Bartholomew's Hospital—there was no protection at all, even when only one M.L.D. was given. Moreover, in animals surviving after inoculation of any of these strains, there was always an abscess at the site of inoculation; whether the survival occurred after a sublethal dose or the life had been saved by antitoxin. Occasionally, such abscesses were absorbed without breaking down, but more frequently they ruptured, often leaving a large slough which healed slowly; hence the name *C. ulcerans* given to the group by American workers. Speaking generally, the post-mortem appearances of animals succumbing to these organisms resembled those after inoculation with *C. diphtheriæ*, but it was found that, when diphtheria antitoxin was able to save the life of the animal with certainty, when two or more M.L.D. broth cultures were given the suprarenals were usually red, as after inoculation with *C. diphtheriæ*; whereas, when no protection was given against one M.L.D. or when protection was uncertain if more than one M.L.D. was given, these glands were usually pale, as after inoculation with *C. ovis*. Thus, the difference in the degree of protection given by diphtheria antitoxin was found to be linked with the presence or absence of changes in the suprarenals and suggested the division of the group into two subgroups. Just recently some high-titre *C. ovis* antitoxin had kindly been given to her by Dr. Carne. This had made it possible to demonstrate further the difference between the two subgroups and also to show the close relationship of one to *C. ovis*. Subcutaneous inoculations were made with forty-eight hour broth cultures of two representatives of each subgroup, with and without enough *C. ovis* antitoxin to neutralize 500 M.L.D. *C. ovis* toxin. The result was exactly the reverse of that when diphtheria antitoxin was given. *C. ovis* antitoxin saved the life of the animals, when strains were given against which diphtheria antitoxin gave little if any protection, but failed to give any protection against those for which diphtheria antitoxin protected. In the case of the former, the amount of *C. ovis* antitoxin given protected against as much as six M.L.D. of the broth culture and possibly the limit of protection was not reached.

These experiments suggested the examination of exotoxins and this had been carried out chiefly by Dr. Petrie and Dr. McClean. But apart from these, the experiments with the living organism had shown that a group of organisms isolated from the human nosopharynx differed not only in some of their cultural and biochemical characters from typical *C. diphtheriæ* but also in their pathogenic effects on guinea-pigs and in their immunological relationships. The group was not a homogeneous one; about equal numbers of the strains isolated in this country were more closely related to *C. diphtheriæ* on the one hand or to *C. ovis* on the other. The occurrence of a lesion at the site of inoculation, even when the life of

the animal was saved by the appropriate antitoxin, showed that exotoxin was not the only factor concerned in the pathogenicity. This factor was found in both sub-groups and, as had been emphasized by previous speakers, it played an important part in the pathogenicity of *C. ovis*. At the same time, neither the American workers nor she (Dr. Barratt) herself had noted with these strains the chronic progressive lesions in the glands and internal organs commonly found after sublethal doses of *C. ovis*.

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Dr. D. McClean said that experiments carried out by Dr. Petrie and himself had revealed a relationship between the toxin of *C. ovis* and the toxins produced by the aberrant diphtheroids which Mrs. Barratt had isolated from the human nasopharynx. The intracutaneous lesions in the rabbit and the guinea-pig caused by the toxins of *C. ovis* and the unusual diphtheroid strains resembled each other and were unlike the Schick reaction produced by the toxin of *C. diphtheriæ*. The rabbit was more susceptible than the guinea-pig to an intracutaneous injection of the toxins of *C. ovis* and the aberrant diphtheroid strains. Cross-immunity tests by the intracutaneous method in the rabbit with sera prepared from horses that had been immunized with the toxin of one of this group, *C.* "*Quitman*," and with the toxin of *C. ovis*, indicated that there was a mutual relationship; on the other hand, the toxin of *C.* "*Quitman*" which was neutralized by the homologous antitoxin, was unaffected by diphtheria antitoxin. Dr. Petrie and himself (the speaker) were unable to distinguish between the toxins of the various members of the group of diphtheroids described in 1933 by Dr. Barratt. The lesions that followed intracutaneous injections of bacterial suspensions were mitigated, but not wholly suppressed, by the antitoxic sera that they had prepared for the purpose of this work.

Dr. Barratt had discussed the relation of the strain isolated by Dr. Mair to the diphtheroids of the "Quitman" group. Dr. Petrie and himself had immunized horses with the toxin produced by this strain in broth cultures; the sera were used in prophylactic and curative experiments. In addition, groups of guinea-pigs had been immunized with toxoid obtained from toxic filtrates, and the immunity thus conferred was compared with that which was produced in similar groups of animals by immunizing them with the toxoid of *C. ovis* and of *C. diphtheriæ*. The results obtained indicated that Mair's strain occupied an intermediate position between *C. diphtheriæ* and the group which contained Dr. Barratt's aberrant diphtheroids and *C. ovis*. Mair's strain appeared to form two toxic components, one of which was identical with diphtheria toxin, whereas the other had an affinity with a toxic constituent of *C. ovis*. The observations of Gilbert and Stewart in New York, of Dr. Barratt, and of Dr. Petrie and himself (Dr. McClean), suggested a close relationship between *C. ovis* and the members of the group of diphtheroids of human origin under discussion.

Professor J. C. G. Ledingham raised the question of the source of those Preisz-Nocard-like strains which had been isolated from the human nasopharynx in this country and America and appear to possess some degree of pathogenicity for man, if one might judge from the clinical condition with which they had been associated.

Further experience only would tell whether such strains might be found responsible for certain diphtheria-like conditions which were alleged to be

uninfluenced by diphtheria antitoxin. It would be desirable to explore thoroughly the possibility that these aberrant strains might reach the human nasopharynx from bovine sources, and perhaps, from milk.

Alluding to the value of the rat-pathogenicity test in distinguishing *C. diphtheriæ* from the Preisz-Nocard type and certain of the human aberrant strains: whereas intraperitoneal inoculation of rats with small doses of Preisz-Nocard led to fatal septicæmia, inoculations of large doses of *C. diphtheriæ* by the same route were readily borne.

Mr. W. A. Pool said that in discussing infection at shearing, emphasis should be laid on the conditions that applied to this procedure when very large numbers of sheep had to be dealt with in extensive farming as carried out overseas. In Great Britain a farm carrying 3,000 head of sheep was considered to be large; in some of the newer countries such a farm was quite a small undertaking. Persons not conversant with the conditions might fail to realize the extent to which opportunity for infection had to be guarded against.

In this extensive farming, the shearers travelled round from station to station and did the work at contract rates, using permanently installed machine power. They sheared a sheep in two or three minutes, and the close herding necessary to pass the sheep through the sheds rapidly, the handling, the shearing—which entailed cuts in the skin in a good many of the sheep—the passage down chutes out of the sheds, etc., led to heavy infection of any raw surfaces with pus from superficial *C. ovis* abscesses that might have burst or been burst, and also with fæces and dust. Close attention was now being paid to opportunities for infection to occur in the course of sheep husbandry operations, and the Australian workers had taken very active steps to deal with the problem.

Section of Neurology

President—S. A. Kinnier Wilson, M.D.

Clinical Meeting at the National Hospital, Queen Square, London, April 19, 1934.

Subacute Combined Degeneration of the Cord.—L. V. Snowman, M.B.

The patient, a woman aged 45, has suffered from pernicious anæmia since April 1929. Treated with liver extract but sometimes neglected to take it.

September 1931.—R.B.C. 2,350,000, rising to 3,475,000 and hb. 72% after six weeks' liver treatment, and to 4,350,000 and hb. 79% after another six weeks' treatment.

November 1931.—Profuse slumber-sweats over thorax; tingling of fingers of right hand; difficulty in walking. Within a fortnight sensory loss to light touch and pain, extending to right elbow and left wrist, right calf and left ankle. Loss of vibration sense in both legs. Astereognosis, incoördination of arms and legs; (?) extensor plantar reflex on right, flexor on left. Marked Rombergism and complete inability to walk. Treated for two months with raw liver without effect.

February 1932.—Treated with 150 gr. Blaud's pill daily. In four weeks practically all symptoms—except slumber-sweats and anæsthesia of terminal phalanges—disappeared. When, however, the liver was reduced to ½ lb. twice a week, R.B.C. count fell to 3,400,000; hb. to 68%. Full dosage of liver recommenced.

August 1932.—R.B.C. 4,100,000, hb. 86%. Tingling in fingers returned when iron was dropped to 30 gr. daily.

November 1933.—R.B.C. 4,712,000, hb. 102% (raised by iron).

Cerebrospinal fluid.—Colloidal gold 0000000. Wassermann reaction negative; globulin and total protein not increased. *Test meal.*—Complete achlorhydria.

Slumber-sweats persisting. Loss to pin-prick over terminal phalanges both hands. Vibration sense absent over sacrum and up to 2 in. above highest point in iliac crests over the spine. (?) Extensor plantar reflex on right side. Some degree of cardiac incompetence, pulse 100 resting. No other symptoms.

The liver was as ineffective to control the development and progress of the subacute combined degeneration of the cord, as was the iron to check the course of the pernicious anæmia.

The case is shown to support Sargant's thesis that the treatment of pernicious anæmia complicated by subacute combined degeneration requires iron to obviate the nervous symptoms, and liver or gastric tissue to keep the blood-count at its proper level. This patient was tried by liver alone, and by iron alone, and in both instances either one or the other of the diseases returned. Since she has been kept on both she has remained in perfect health. The diagnosis was confirmed by Dr. Gordon Holmes three years ago.

Discussion.—Dr. F. PARKES WEBER said that the worst case he knew of that had been treated successfully by Dr. W. Sargant's method of massive doses of iron, was in a woman, aged 51 years, admitted in June 1933 to the German Hospital under the care of his colleague, Dr. E. Schwarz. She had pernicious anæmia with combined degeneration of the cord. The case was complicated by a very severe bed-sore, but she was now getting about again.

Dr. GORDON HOLMES said that when he first saw this patient she was confined to bed, and was able to take only two or three steps with support. Her hands were very numb and awkward in movement. She had had liver treatment but had not responded by any improvement in her nervous symptoms. After iron treatment was instituted the amount of recovery which members had seen took place. She had all the characteristic signs of very severe combined degeneration of the cord; there could be no doubt of this diagnosis. There was no suspicion of a psychogenic element in the case.

The PRESIDENT said that such a case as this was important therapeutically, as most neurologists had been critical of the treatment of subacute combined degeneration, and had been dissatisfied with the use of either liver alone, or other substances alone. The combined method apparently produced impressive results. The contrast between the original and the present conditions in this case was surprising.

(?) Schilder's Encephalitis.—J. STC. ELKINGTON, M.B.

J. H., aged 11½.

Chief features on examination: Loss of memory without any other deterioration of mentality, blindness associated with bilateral consecutive optic atrophy, and signs of bilateral disease of the pyramidal tracts.

Family history.—Father and mother alive and well. Collaterals healthy. Three sons in family: (1) L. H., aged 15, now well, but in July 1933, while working for an examination, had developed involuntary movements down the right side of the body. These rapidly grew worse; arm and leg were weak. The condition was considered to be chorea and after three weeks in bed the boy recovered. On examination now, he appears to be normal except for diminution of the abdominal reflexes and accentuation of the knee-jerks on the right side. (2) R. H., aged 13, quite healthy. (3) J. H., the patient.

Past history.—Whooping-cough at age of 4 years; measles at age of 6. No other illnesses. Has always been a quick, vivacious child, but in spite of his intelligence has never had a retentive memory.

History of present illness.—August 1932. When aged 10, developed within a few days, weakness of the left arm. The left leg dragged and the left corner of the mouth drooped. There were no other symptoms. He was in hospital for nine weeks. The cerebrospinal fluid was normal and he recovered completely.

January 1933.—Face began to twitch, especially on the right side. Chorea was diagnosed. Condition improved on treatment.

June 1933.—Went to camp. Was not quite well. Had moods of hilariousness and sleepiness.

September 1933.—Involuntary movements returned and were more severe. Patient was kept away from school.

December 1933.—Sudden onset of severe headache and pain over right eye. Next morning he awoke with complete blindness of the right eye which has persisted. Three weeks later he awoke with blindness of the left eye, without pain. This too has persisted.

Admitted to Plymouth Hospital.—Headache and vomiting occurred frequently. Slight pyrexia. He was completely blind. Both discs showed slight swelling but were of normal colour. No abnormal signs in central nervous system recorded. Cerebrospinal fluid (examined on two occasions), normal. X-ray examination: Skull and accessory sinuses, normal. On discharge the condition was unchanged.

Admitted to St. Thomas's Hospital, 21.2.34.—*Mental state*: The boy is cheerful and of a charming disposition. He appears to be quite indifferent to his misfortunes. He answers questions and takes part in conversation intelligently but shows severe defect of memory for both recent and remote events. Emotionally he is stable. Neither headache nor vomiting has occurred. He is afebrile.

Cranial nerves.—The right eye is completely blind; the left has faint perception of light. The right optic disc is very pale from post-neuritic atrophy; no perceptible swelling. The left optic disc is also pale from post-neuritic atrophy and shows some distension of the capillaries and the disc edge is obscured. Swelling about 2 D. Retinal arteries not obviously reduced in either eye. Pupils equal in size and circular. Both react subnormally to direct and consensual light and better upon convergence. There is possibly a slight left facial weakness but in other respects the cranial nerves are normal. Hearing normal.

Motor system.—Upper extremity: Normal. Lower extremity: slight increase in tone in left leg but otherwise normal; gait when first seen was groping and uncertain in nature but not otherwise abnormal.

Sensation normal throughout.

Reflexes.—Arm-jerks normal. Abdominal reflexes normal. Knee-jerks and ankle-jerks brisk, especially on left. Plantar reflexes: right flexor, left doubtful.

Since admission the boy's mental condition and sight have remained substantially the same but there has been a gradual increase of disability in the legs. Both are now slightly spastic and the plantar response is extensor on each side. His gait is spastic. The pupils have become progressively less active to light.

Lumbar puncture has not been repeated.

There is no doubt that there was papillitis in both eyes at one stage of the illness though it is no longer present.

Discussion.—The PRESIDENT said that the condition might be disseminated sclerosis. Had the possibility of cerebral tumour been considered?

Dr. ELKINGTON (in reply) said he was satisfied that the onset of the blindness had been sudden and complete, and there had been no evidence of recovery since; this was unusual in disseminated sclerosis, and the age of the child was also against that diagnosis. He assumed that the original attack of weakness was a cerebral, not a spinal, illness, as the face had been involved, as well as the arm and leg. A striking feature was the mental change; there had occurred a marked loss of memory for both remote and recent events, which indicated extensive disease of the cerebral hemispheres.

With regard to the second point raised: There had been separate lesions in both optic nerves, and disease of both the pyramidal tracts. Such diffuse lesions would not be easy to explain on the basis of tumour, and the patient had no headache or vomiting, or other classical sign of tumour.

The PRESIDENT asked whether it was usual to find peripheral lesions in a case of Schilder's encephalitis.

Dr. ELKINGTON said that in three reported cases papillœdema had been present.

Sir JAMES PURVES-STEWART asked whether the exhibitor would consider the advisability of pneumo-radiograms so as to eliminate the possibility of a gross intracranial mass.

Dr. ELKINGTON replied that the prospect of carrying out useful treatment would not be great, and the method did not appear to him to be justifiable in this case.

Spastic Paraplegia. (?) Pyramidal Degeneration: Case for Diagnosis.—J. STC. ELKINGTON, M.B.

G. L., a boy aged 11½, was normal till the age of 5 years. He then began to be "heavy on his legs," and to "stumble and kick the mats." The legs tired easily, trembled and dragged. They were equally affected.

The condition has gradually become worse. There have been no other symptoms except slight precipitance of micturition ; this has disappeared during the past six months.

Past history.—Measles when aged 2½, followed by pneumonia. Was in hospital three months. Is stated "never to have been the same since."

Family history.—One sister, aged 8, healthy. No nervous disease in family.

Present condition.—A healthy, well-developed boy of normal intelligence. Cranial nerves, upper extremities, and trunk are all normal except for accentuation of the tendon reflexes in the arms. The legs show a mild spastic paraparesis with increased tendon reflexes and bilateral extensor plantar responses. No definite sensory loss, but a subjective diminution of sensibility to pin-prick has been observed from L 1 to L 3 on each side at each examination.

Investigations.—Cerebrospinal fluid normal in all respects. Blood-Wassermann reaction negative. Queckenstedt test negative. Skiagram of spine, normal.

I ask for suggestions as to diagnosis. It seems to be a case of progressive paraplegia in which apart from slight sensory disturbance about the upper lumbar segments there is no evidence of spinal compression. I think it is a degenerative condition of the pyramidal system, of the abiotrophy type, but that is an unsatisfactory diagnosis.

The PRESIDENT said that there was also a suggestion of nystagmus ; when the eyes were put into a lateral direction and the patient was asked to sustain the movement, one noticed a flickering. He (the President) considered that there was more than a spastic paraplegia alone.

Cerebral Cysticercosis : Paroxysmal Hydrocephalus. — MACDONALD CRITCHLEY, M.D.

A. Y., aged 31, served as a regular soldier in India after the War. No history of infection with *Tænia solium.*

His present illness began with periodic headaches in 1930. In October 1932, whilst driving his lorry, he suddenly saw double and the right side of the body became numb. He became muddled but not unconscious. Severe headache and vomiting followed. For the next day or two he was very ill with headache, stiffness of the neck and frequent epileptiform convulsions. The abdominal reflexes were absent. The symptoms were relieved by lumbar puncture. No abnormal signs were present a fortnight later.

Ten days afterwards a similar though slighter attack occurred, and two days later diplopia was still present on the extreme right, there was ocular deviation and the knee-jerks were sluggish. He was admitted to hospital, where some nystagmus and weakness of the right face and tongue developed. Other similar attacks of headache, vomiting, diplopia and convulsion occurred.

In February 1934, the neurological signs were unchanged.

X-ray examination of the muscles revealed a large number of calcified cysts. A skiagram of the skull showed prominent vascular markings only. No subcutaneous nodules were felt.

We are now becoming more familiar with this condition. At the last Clinical meeting of the Section two of these cases were shown, and, as I mentioned then, the authorities at Millbank have been able to collect over 70 cases of the disorder.[1]

This patient is instructive for two reasons. Firstly, because his recurrent attacks are not essentially of epileptiform nature, but are rather attacks of sudden severe hydrocephalus. He becomes very ill for a week at a time, with intense prostration, headache, vomiting, diplopia and convulsion. Secondly, this patient is instructive because clinically he shows no signs of cysticercosis, no subcutaneous nodules being palpable.

[1] *Proceedings* 1934, xxvii, 667-669 (Sect. Neur., 19-21)

Discussion.—Sir JAMES PURVES-STEWART said he presumed that, though there was no doubt about the diagnosis, the exhibitor would carry out additional confirmatory observations. Both the cerebrospinal fluid and blood should be examined for the presence of eosinophilia and for the specific cysticercus antigen reaction.

Dr. PURDON MARTIN asked whether radical therapeutic measures had been carried out. He was thinking of X-ray or radium treatment.

THE PRESIDENT said he did not see any cysticerci in the skiagrams of the skull. What was of neurological interest was the site of the lesion which was causing these recurrent attacks. Was the lesion in the ventricle? If Dr. Critchley had the opportunity of examining the patient during or just after an attack, he should pay special attention to the possibility of ectopia pupillæ.

Dr. CRITCHLEY (in reply) said that the man was still an out-patient, but when he came into hospital a blood-count and a complement-fixation would be carried out. There was only one source of supply of antigen in London and it was difficult to procure. The patient had already had treatment both with X-rays and radium.

Peroneal Muscular Atrophy.—N. S. ALCOCK, M.B.

Aged 30. Admitted to National Hospital 28.3.34, under Dr. F. M. R. Walshe.

Family history.—No history of similar complaint could be obtained. Patient is the seventh of nine children; four died in childhood (cause not known). The rest are perfectly well. There was no blood-relationship between the parents.

Personal history.—His legs have always been a "little queer" and he has always had a peculiar gait and a slight limp. He thinks his legs have grown thinner just below the knee during the last three or four years. Otherwise well till four or five years ago when he became rather "nervy." Three years ago noticed that his right forearm was getting weaker and thinner and had twitching of the fingers. Steady progress till present time. Left hand and forearm, probably, for as long—but he has not noticed them so much. Has noticed occasional flickering of the muscles.

On examination.—Marked symmetrical wasting and weakness of both forearms and legs, extending up to elbows and knees respectively. Wasting ends abruptly here. Occasional fibrillary tremors in small muscles of the hands. Gait: high stepping with slapping down of feet. No ataxia. Reflexes: Tendon-jerks absent on both sides. Abdominal reflexes present; plantars flexor. Cerebrospinal fluid normal.

Mental state: History of nine months in mental home; now shows schizophrenic tendencies.

Discussion.—Dr. MACDONALD CRITCHLEY said he had seen this combination of peroneal muscular atrophy and schizophrenia in a patient once before, at Broadmoor.

The PRESIDENT said that such cases were not very rare, and in the *Review of Psychiatry*, in 1905 there had appeared a paper by McFie Campbell, Professor of Psychiatry at Hertford U.S.A., dealing with cases of the associated conditions.

Familial Presenile Dementia.—E. GRAEME ROBERTSON, M.D.

C. G., male, aged 53. Admitted to the National Hospital, Queen Square, on March 19, 1934, under the care of Dr. Critchley.

This patient's case, together with a very complete family history, has been reported in detail by Dr. Worster-Drought, Dr. Hill, and Dr. McMenemey in the *Journal of Neurology and Psychopathology* (1933, xiv, 27).

History.—In 1928 the patient was noticed to become increasingly forgetful and unduly irritable. He commenced to "splutter" when he talked, became unsteady on his legs and at a later date his feet dragged when he walked. He became more and more apathetic and fifteen months ago incontinence of urine and fæces commenced. He sat or lay where placed, passed urine and fæces underneath him, and neither spoke nor moved spontaneously.

On examination.—Gross mental defect, confusion and disorientation, with little power of recalling past and recent events. Sometimes, when pressed for an answer, he confabulates. Perseveration marked. Spoken speech limited to a few words, gross slurring dysarthria with bad spacing of syllables. No real apraxia but he uses his right hand more freely and, to command, more accurately than his left. His upper limbs perform a series of restless movements, often of a vaguely exploratory nature, most marked in the left hand, which although not exhibiting a definite grasp reflex, frequently includes the fingers of his other hand, his bed clothes, etc. There is almost complete absence of any spontaneous activity, but he has again learned to feed himself. He has shown no emotional reaction of any sort during his stay in hospital.

The presence of voluntary movements and resistance to passive movement makes the tone of the arms difficult to estimate. Almost complete relaxation can be secured. His legs are held rigidly in extension, often with great toes dorsiflexed, and only slowly return to this posture from any other imposed upon them. On this account it is difficult to estimate tone; there is marked resistance to passive movement in any direction, most marked at the commencement of flexion.

Calf and quadriceps femoris muscles show fibrillary tremors. All deep reflexes, including the jaw jerk, are extremely brisk. Bilateral ankle clonus, brisker on the left, abdominal reflexes present. Plantar responses flexor. Gait uncertain and unsteady; legs moved very rigidly. No gross incoördination. Sensation normal. Blood-pressure 100/60. Cerebrospinal fluid: Initial pressure 150 mm.; no cells. Total protein 0·110%; Pandy, weakly positive; Lange, no change. Wassermann reaction negative.

Immediate family history.—Maternal grandmother suffered from a similar complaint. She married a healthy man and had ten children. The eldest was normal; the succeeding six were all affected, and the youngest three, born while their mother was ill with the disease, lived to a healthy old age. The mother of the patient was the third child of this generation. At the age of 46 she became irritable, apathetic and disinterested. One day she suddenly had difficulty in speaking, and after that spoke in a spluttering kind of way and dragged her feet when walking. Later she sat in a chair all day, and would neither wash nor attend to her bodily needs. In 1905 she was examined in the out-patient department of this hospital by Sir Farquhar Buzzard, when, at the age of 50, she was dull, heavy and lethargic, "with defective memory for recent events. There was articulatory defect, her arms were weak, and she walked in uncertain manner." She died when aged 54.

She had seven children. (1) E. S., female, twice admitted to this hospital, in 1924 when aged 45, and in 1926. Six months before her first admission she tried to get out of bed one morning and found she could not stand or talk properly. She was emotional, with poor memory and marked dysarthria. Reflexes normal. Blood-pressure 138/95. Cerebrospinal fluid normal (total protein 0·03%). From that time onwards "she just sank away, did everything where she lay," and died when aged 54.

(2) The patient, C. G.

(3) H. G., male, died from double pneumonia, aged 38. Unaffected.

(4) M. G., female, now aged 46. Her husband states that her memory has been failing for recent events; she is unduly irritable, cannot concentrate, and will not read; she hesitates and sways when she walks, and stumbles over difficult words.

The remaining three siblings, aged 43, 39 and 36, are at the present time quite well.

In their account of the case the authors referred to the defect in the limb as being an extrapyramidal rigidity, and I wonder whether they meant that the basal ganglia were involved. May it not be that the lesion is at the cortical level, associated as it is with the mental deterioration of the patient? The exploring movements of the left hand, the tendency to grasp, the slight degree of catatonia and the resistance to passive movement may be indicative of a lesion of the pre-Rolandic cortex.

Discussion.—Dr. C. C. WORSTER-DROUGHT said that the patient's condition was evidently slowly deteriorating: since last year both the spasticity and degree of dementia had become more profound. In an extensive search of the literature he and his colleagues had failed to find an exactly similar condition described. In the spasticity, dysarthria and dementia, the disease resembled Jakob's pseudo-sclerosis, but it differed from that disorder in the absence of tremor and of spontaneous movements. In the recorded cases of Jakob's pseudo-sclerosis, tremor had been an early and pronounced feature. Spastic paralysis of both a pyramidal and extrapyramidal type had also been described in a few cases of Pick's disease; in the examples recorded the spasticity appeared to have developed only at a late stage, that is, long after the onset of dementia. In only one case in the patient's family had the mental disturbance preceded the paralysis. In neither Pick's disease nor Jakob's pseudo-sclerosis had any pronounced family history been described. In the latter condition there had been no striking hereditary feature, while in Pick's disease only a few familial examples had been recorded, e.g. by Grünthal[1] in two brothers, and also in two sisters, one of whom had a child similarly affected. Urechia[2] stated that heredity played only a minor part in Pick's disease, and that familial cases were very rare.

The PRESIDENT said this case was not quite like any he had seen before. The degeneration must be widespread. It was pyramidal, extrapyramidal, and much more. Was it an involutional state, pre-senile, particularly of a widespread kind? It seemed to involve the major portion of the projection systems as well as the association systems. Any opportunity of a pathological examination of such a case would be of extreme value.

Neoplasm (? Nasopharyngeal Endothelioma) of base of Skull producing Unilateral Paralysis of the 9th, 10th, 11th, and 12th Cranial Nerves.—JOE PENNYBACKER, M.B.

Mrs. E. M., aged 42. Admitted to hospital, 26.3.34, under the care of Dr. Grainger Stewart.

History.—Ten years ago, began to complain of severe intermittent pain in region of left ear. Seven years ago, her voice became weak and husky, she had some difficulty in swallowing and occasional nasal regurgitation, and the left side of the neck began to waste. Five years ago she was in this hospital, when a tumour was discovered in the interval between the left angle of the jaw and the tip of the mastoid process. A course of deep X-ray treatment to the region gave her some relief from the pain in the ear. Six months ago, the pain became much worse, spreading over the left cheek, down the left side of the neck, and up the back of the head on left side. She had frequent attacks of giddiness and vomiting.

On examination.—A thin, wasted-looking woman (she says that her appearance has not altered much during the past five years). Firm, rounded swelling in interval between left angle of jaw and tip of left mastoid process; fixed deeply; not tender. No palpable enlargement of cervical lymph-glands. Enophthalmos of left eye. Left pupil smaller than right. Pupillary reactions normal. Impairment of taste left side of tongue. Slight middle-ear deafness of left ear: granulomatous mass just visible in depth of external auditory meatus. (Biopsy of a similar mass two years ago: "myxomatous polyp.") Left pillars of fauces thin and atrophic. Palate elevates to right on phonation. Retch reflex impaired on left side. Left vocal cord fixed.

Extreme wasting and proportional weakness of left upper trapezius and sterno-mastoid. Tongue protruded to left: wasting on left half.

Limbs normal. No evidence of any abnormality in chest or abdomen. Blood-count normal. Wassermann reaction negative in blood and cerebrospinal fluid.

This case was felt to be interesting chiefly from the point of view of the nature of the neoplasm. The tumour has been present for five years; when the patient was in hospital two years ago it was of much the same size and consistence as now, the physical signs were the same. Most of the cases of nasopharyngeal endothelioma

[1] GRÜNTHAL, E., *Zeitsch. f. d. g. Neurol. u. Psychiat.*, 1926, c, 128.
[2] URECHIA, C. J., *L'Encéphale*, 1930, xxv, 728.

which have been reported have run a more rapid course than this, and have been peculiarly unsatisfactory in regard to response to treatment. I think treatment with radon seeds has given the best results. This case has responded satisfactorily to deep X-rays. There has been little change since the patient came to hospital, except that the vomiting and attacks of giddiness, which formed the predominant symptoms on readmission this year, cleared up completely without any specific treatment.

Discussion.—Mr. GEOFFREY JEFFERSON said he thought from the history the lesion could not possibly be nasal endothelioma as usually understood, and of which he had seen many cases. In all the growth had been more anterior than that in this case. Further, he had never seen one which did not begin at the 5th nerve, or, at least involve it, whereas in this case the involvement began as a 9th nerve palsy. He did not regard this growth as a "University College Hospital tumour" (so-called because it had been well-worked out there). New, of the Mayo Clinic, had also worked out this kind of tumour. He (Mr. Jefferson) regarded this as a basal endothelioma. He understood that it was radio-sensitive, and that was a remarkable feature of this particular type. The treatment almost universally employed was deep X-ray therapy, not implantation. Under this therapy the tumour melted away. Death in these cases occurred, almost always, from intracranial extension. With a vertical projection of the skull one could see in a skiagram the erosion of the floor of the skull. With increasing knowledge of what could be done and where the fault lay, the technique might be improved.

Dr. PENNYBACKER (in reply) said that no abnormality in the skull was detected by X-rays, though antero-posterior and stereoscopic views were obtained.

Tabes Dorsalis, with Complications.—MACDONALD CRITCHLEY, M.D.

Male, aged 47, contracted syphilis in 1912. He was given three injections of salvarsan, and then regarded as cured.

For some years he has complained of weakness and pains in the arms. Soreness of the tongue was noticed a year ago. More recently he has felt weak and breathless. He also complains of occasional attacks of irresistible sleep.

On examination.—Glossitis; fœtor; ozæna. Enlargement of liver and spleen. Bilateral swelling and ankylosis of elbow-joints. Periostitis of shins, especially the left. Pupils equal; reactions normal. Knee-jerks, right greater than left; ankle-jerks unequal; both sluggish. Blunting to pin-prick across chest and over nose. Heart: slight enlargement; aortic systolic and diastolic murmurs. Blood-pressure 115/70. Pulse-rate slow.

Pathological findings.—Wassermann and Kahn reactions + + (Blood).

Cerebrospinal fluid: 5 cells per c.mm. Total protein 0·06%. Wassermann reaction negative. Lange negative. Pressure 160 mm.

Urine: albuminuria; pus present.

Blood-count: R.B.C. 4,320,000. Hb. 52%; C.I. 0·6; W.B.C. 16,600. *Differential.*—Polys.: neutros. 67·5%, eosinos. 2·0%, basos. 1·8%; lymphos. 23·0%; monos. 6·5%.

X-rays: Generalized syphilitic osteitis of skull, tibiæ and humeri. Arthritis both elbows.

I think this case would have been better labelled "complications with slight tabes." The textbooks emphasize the rarity of the combination of visceral and cutaneous syphilis with neurosyphilis, but one has been in the habit of teaching that in tabes one looks for evidence of syphilis in three places—the aortic region, the tongue, and the shins. This patient shows, in addition to slight tabes, glossitis, periostitis of the shins, aortic disease, enlarged liver and spleen, osteitis of the skull, a renal infection, bilateral arthritis, tertiary syphilitic osteochondritis of both elbow-joints; moreover, he is anæmic and has a rash. When I saw him first he had slight mercurial poisoning too.

Discussion.—The PRESIDENT said that the patient was also somewhat feministic, in other words, emasculated, and it would be interesting if Dr. Critchley could investigate that point from the endocrine point of view, as the man was a perfect museum of syphilis. It was rare in these days to find syphilitic osteitis of the cranial vault; he had not seen that condition for years.

Dr. STOLKIND, remarking on the enlargement of the liver and spleen in this case, said that out of his 132 cases of syphilitic aortitis with post-mortems there were only two of syphilis of the liver (*Med. Press and Circ.*, 1921 and 1922).

Pituitary Basophilism.—S. P. MEADOWS, M.D.

Mrs. L. K., aged 38 (patient of Dr. George Riddoch).

History.—Six years ago had rheumatic fever and was in bed for three months. Her present symptoms date from that time. She has had hypertensive headaches, transient attacks of giddiness, palpitations and dyspnœa on exertion, and œdema of the feet at night for the past six years. She has also had generalized aching pains in her joints, limbs and trunk. Six years ago her face began to get fat and florid and hairs began to grow on the chin and upper lip. She now shaves once monthly. Her weight increased from 8 st. 9 lb. to about 13 st., but is now about 11½ st.

She has bruised easily for the past six years, and frequently has spontaneous ecchymoses on her limbs. Sometimes her eyes become red and bloodshot (conjunctival ecchymoses).

Amenorrhœa for about six years.

On examination.—Florid face, with moderate degree of hair-growth on upper lip and chin, and slight hair-growth over cheeks. She is obese, the obesity being confined to the trunk. The limbs are rather thin in comparison.

There are numerous cutaneous striæ over the skin of the abdomen and upper thighs (fig. 1) and over the posterior axillary folds.

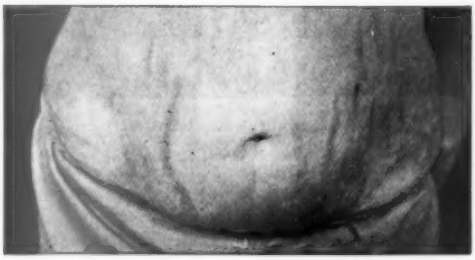

FIG. 1.—Showing cutaneous striæ.

No excessive hair distribution over the trunk, but hair is slightly increased over the arms; axillary and pubic hair normal. Hair of scalp falling out (X-ray treatment).

Ecchymoses are frequent in the arms and legs. The skin of the legs below the knees is thick and rough, and shows a patchy brownish pigmentation and several ecchymoses (fig. 2). Occasionally conjunctival ecchymoses develop. No abnormal physical signs in the central nervous system. Pelvic organs and external genitalia normal.

Heart slightly enlarged to left; aortic second sound accentuated; occasional extrasystoles. Blood-pressure 230/130.

Urine: sp. gr. 1018; albumin present; no casts. Blood-urea 40 mgm.%. Urea concentration test: No evidence of renal inefficiency.

Bleeding time and coagulation time normal. Platelet count: 410,000 per c.mm. Glucose tolerance test: normal. Blood-calcium 10 mgm.%. Blood-phosphorus 2·08 mgm.%.

Skiagram of wrist compared with that of normal person: No evidence of decalcification. Skiagram of skull: posterior clinoid processes appear indistinct,

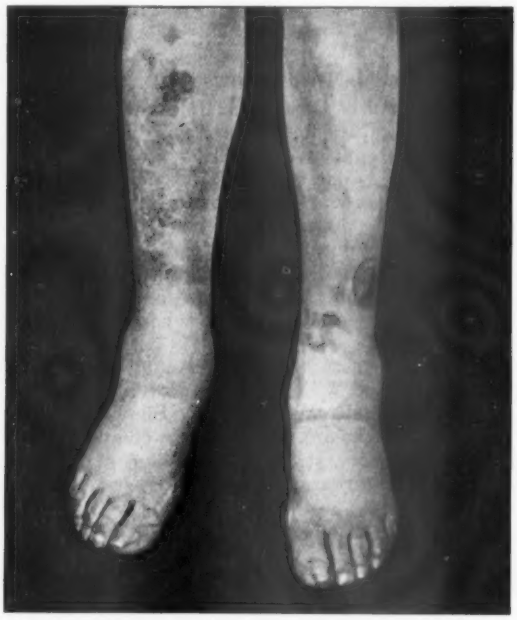

FIG. 2.—Showing pigmentation of legs.

? early erosion. No enlargement of sella. Skiagram of renal area: no calcification seen, but there is an old fracture of left lower rib and a crush injury to the first lumbar vertebra.

22.3.34.—Fracture of surgical neck of right humerus owing to a fall.

Discussion.—Dr. PARKES WEBER said he thought that this was one of the most typical cases of the condition, from the clinical point of view, which had ever been shown in England.

It almost exactly resembled the case which he (the speaker) had published in the *British Journal of Dermatology* in 1926 (xxviii, pp. 1 to 19); in his case the patient was younger, and the symptoms were more acute. She died with acute pulmonary œdema. Dr. F. E. Loewy, present at this evening's meeting, was the house-physician of the case at the time. Dr. Weber directed attention to the appearance of the present patient's legs; it was due to superficial hæmorrhages with resulting pigmentation and trophic changes in the skin; this was one of the most important features of Cushing's syndrome.

All that, however, did not prove that a minute basophil adenoma of the pituitary gland was the primary cause of the symptoms. The adenoma-formation might represent reactionary functional activity (cf. F. P. Weber, *Med. Press*, 1933, clxxxvii, p. 568). This question would ultimately be settled by making serial sections of every pituitary gland in cases coming to the post-mortem room.

Certain cases of this group had had marked glycosuria, which brought them under the French clinical heading: "diabetes mellitus in hairy women." In the case of a young woman

at Guy's Hospital shown to Dr. Weber by Dr. A. F. Hurst in 1930, the urine contained both albumin and sugar. That patient died ultimately with acute pulmonary œdema, and by microscopic examination of the pituitary gland a small basophil adenoma was discovered (see P. M. F. Bishop and H. G. Close, *Guy's Hosp. Reports*, 1932, lxxxii, p. 143).

Dr. LOEWY said that this case was strikingly similar to that of Dr. Parkes Weber's patient whom he (Dr. Loewy) had attended for some time before her death from pulmonary œdema. The cases—both in young women with amenorrhœa, obesity, severe hyperpiesia, hard œdema of the legs, striæ, purpura, etc.—belonged to the same definite clinical entity.

Dr. STOLKIND said that a correct diagnosis of pituitary basophilism was very difficult, especially when the sella turcica was normal. There were, so far, no special signs or symptoms of Cushing's pituitary basophil syndrome which would absolutely distinguish it from a genito-adrenal syndrome.

Mr. G. JEFFERSON, referring to examination of the pituitary gland, said that Dr. Susman, of Manchester, in his series of routine examinations in the post-mortem room, which would shortly be published, had found at least a dozen basophil adenomata in cases which had shown no signs of basophilism at all.

Cranial Nerve Palsies (? Aneurysm of Internal Carotid Artery).—S. P. MEADOWS, M.D.

Mrs. M. B., aged 46. (Patient of Dr. G. Riddoch.)

History.—Six months ago: Onset of aching pain behind left eye, which later spread to left infraorbital region, left temple and left side of forehead.

This has persisted, but has been less severe recently.

Six months ago: Onset of diplopia, and left eye turned inwards.

Two and a half months ago: Vision of left eye became blurred, and this has become worse. "A mist gradually spread upwards over the left eye," so that now she can see things better above the horizontal than below. She has also had a feeling of tightness and numbness above the left eyebrow. The left upper lid has drooped during the past few weeks. She has had impaired hearing in the left ear, with tinnitus, but recently this condition has improved.

On examination.—A thin, middle-aged woman.

Cranial nerves: (1) Normal.

(2) Visual acuity: Right, $\frac{6}{9}$. Left, about $\frac{1}{60}$ (counts fingers). Visual fields: Right, full. Left, peripheral constriction when examined by confrontation tests with large white disc. The remaining field is more distinct above the mid-line than below. Optic fundi: Medial opacities prevent clear view of fundi; left optic disc slightly pale; right normal. Fundi otherwise normal.

(3, 4 and 6) Pupils of moderate size and equal in subdued light, almost circular. Left pupil fixed to light, consensual and direct. Left eye adducted and turned slightly downwards; left-sided ptosis; slight left-sided exophthalmos.

(5) Left corneal reflex absent. Cotton-wool and pin-prick impaired over first division of left fifth nerve. Cotton-wool slightly impaired over second and third divisions of left fifth nerve. Jaw deviates to left on opening against resistance. Left masseter and temporal muscles weak and wasted slightly.

(8) Air conduction slightly reduced on left, but greater than bone conduction which is normal.

(9, 10) Normal. (11) Normal. (12) Tongue deviates to left when protruded (jaw deviates to left). Taste normal on both sides of tongue.

Limbs: No abnormality. Reflexes: Tendon reflexes depressed. Otherwise normal. Sensation: No abnormality except over left fifth sensory supply. Cardiovascular system: Heart enlarged to left. Blood-pressure 220/130. Arteries thickened and tortuous.

Cerebrospinal fluid: Initial pressure 125 mm.; 4 small mononuclears per c.mm.; total protein 0·055%; Nonne-Apelt and Pandy negative; Lange, no change. Wassermann reaction negative in cerebrospinal fluid and blood. Blood-count normal. Eosinophils 1·5%.

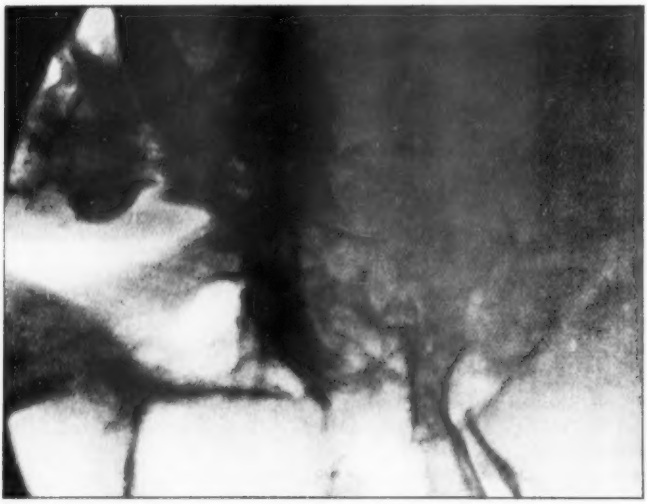

FIG. 1.—Lateral skiagram of middle fossa of the skull, showing the calcified ring, with the pituitary fossa showing through.

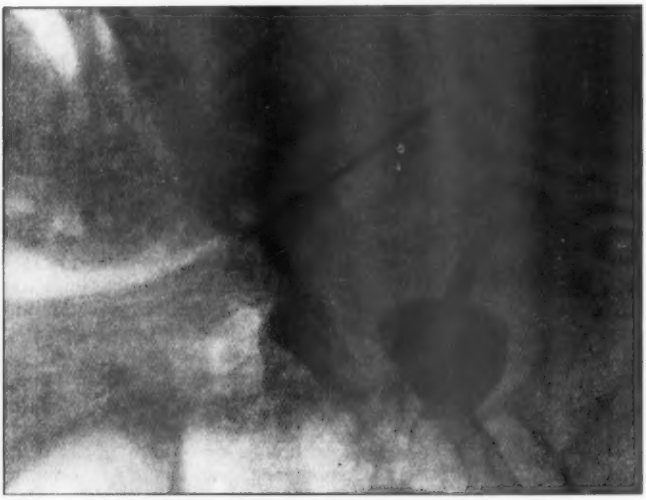

FIG. 2.—Lateral skiagram of middle fossa of skull, after injection of thorotrast, showing the aneurysm filled with the radio-opaque substance.

Skiagram of skull: There is a large mass in the left middle fossa with a calcified wall, with erosion of the lateral wall of the sphenoidal sinus on the left (fig. 1). The sella turcica appears to be normal.

Discussion.—Dr. RUSSELL BRAIN said it was difficult to believe that there could be an aneurysm of the size of this tumour without a bruit being audible—at least to the patient. Had the possibility of hydatid cyst been considered?

Dr. MEADOWS (in reply) said that the lungs had been examined by X-rays and showed no evidence of hydatid cyst.

The PRESIDENT said that the diagnosis in this case seemed to rest largely on the interpretation of the skiagram; he had never seen anything like it. He agreed with Dr. Brain in being sceptical as to aneurysm, when there was only six months' history of such a large mass. Much smaller aneurysms—if this was an aneurysm—in the same place had caused symptoms long before six months. It seemed almost absurd to suggest neoplasm. The calcifications which he (the President) had seen were not so symmetrical as this. Aneurysm was not necessarily circular.

Mr. JEFFERSON said that he sympathized with the views expressed on this case, yet he strongly suspected that the tumour *was* an aneurysm, especially as it was exactly in the situation in which aneurysms were found. Massive aneurysms in the internal carotid had a way of blowing out into the middle fossa. He had seen larger aneurysms than this, with a short history, but not calcified, which had come out into the floor of the middle fossa, almost to the greater wing of the sphenoid. In that type of aneurysm he did not think bruits were heard. This patient had slight exophthalmos on that side, and he (the speaker) had tried to see if it had opened up the sphenoid fissure. He had seen calcified aneurysms in this situation.

POSTSCRIPT.—Since the meeting, thorotrast has been injected into the common carotid artery for the purpose of carrying out arteriography. The aneurysmal nature of the mass was clearly demonstrated by an almost complete filling of the mass with the radio-opaque substance (fig. 2).

Involuntary Movements. ? Torsion Spasm.—D. DENNY-BROWN, M.B.

L. B., aged 20, admitted to Guy's Hospital, under care of Dr. C. P. Symonds, in February 1932, and April 1934, complaining of dragging of the left foot in walking. There is no family history of nervous disease except that one sister developed a neurosis and subsequently recovered. At the age of 13 years, extensive osteomyelitis in the left arm, with operative treatment, resulted in severe disability in movement of the left wrist. No history of encephalitis could be elicited.

In January 1931 the left foot was noticed to become cramped and inverted whenever the patient walked any distance, and about this time the left hand was observed to make trembling movements when at rest. In June 1931 an involuntary turning of the head to the right was first noticed, and from that time disability has gradually increased. Since June 1933 the right foot has commenced to draw inwards in walking, so that now the patient can walk only a very short distance before cramped postures of the lower limb bring her to a standstill.

The head is drawn to the right by a continuous spasm of all the muscles on the right side of the neck. The spasm shows irregular fluctuations which are now less noticeable than when first observed in 1932. The left upper limb is hypotonic at all joints, and the hand tends to assume an athetoid posture. Occasional involuntary movements, more rapid than athetosis, are observed. In walking the limb is extended. The left lower limb shows some contracture in flexion of the hip and some spasm of flexion of the hip and knee and inversion of the foot. This spasm is increased by movement and, like the torticollis, shows irregular fluctuations. Inversion of the right foot may be observed after exercise. The tendon-jerks are brisk and equal, with

the exception of the left supinator jerk which is diminished, probably owing to local scarring. The abdominal reflexes are present, the plantar reflexes flexor. The cerebrospinal fluid has shown no abnormality on two occasions.

Neurofibromatosis, Central and Subcutaneous.—C. WORSTER-DROUGHT, M.D.

F. C., aged 17, first seen in November 1933, complaining of occasional vomiting. His appetite remains good; he has no headache and no epigastric pain. He is able to walk normally for a short distance but after about twenty or thirty yards he feels giddy and has occasionally fallen. Occasional diplopia if reading for some time.

Previous history.—None of importance except that of pneumonia as a young child.

Family history.—Father dead, cause unknown. Mother alive and well; two brothers and one sister, of normal stature, alive and well.

Physical signs.—Speech somewhat slurred. Teeth in good condition but widely spaced; no enlarged glands; chest normal.

Pupils equal; react normally. Fundi normal. Convergent strabismus. Weakness of right external rectus. Nystagmus on looking to left and right and also when looking upwards. Nerve-deafness of right ear. Sensation normal.

Weakness and wasting of intrinsic muscles of right hand and muscles of right forearm. Right arm-jerks brisker than left. Knee-jerks brisk, right slightly greater than left. Ankle-jerks moderate. Abdominal reflexes sluggish. Bilateral extensor plantar reflexes. Slight incoördination of right arm with some tremor of fingers. Ataxia in walking; walks on wide base. Romberg positive. Muscular tone of legs good and equal but bilateral pes cavus.

Many scattered subcutaneous nodules and small fibrous masses, i.e. back, left calf, right calf and in front of right tibia.

Cerebrospinal fluid: Two cells per c.mm.; total protein 0·28%; globulin in moderate excess; Wassermann reaction negative; Lange 3455432110; pressure 220 mm. Queckenstedt positive up to 300 mm.

Blood Wassermann reaction negative. Blood-count: no abnormality.

Biopsy of subcutaneous nodule removed from upper part of back shows a fibroma with some degeneration of the fibres (H. C. Lucey).

Intracranial Aneurysm with Calcified Wall, visible in Skiagrams.—J. PURDON MARTIN, M.D.

J. S., female, aged 49, began, at the age of 17, to have mild epileptiform seizures. These were generalized attacks but they affected the right side more than the left. After twenty years the attacks became localized; they affected the right hand and the right side of the face and sometimes disturbed the speech. They did not cause unconsciousness. These local attacks were preceded by a sensation of severe cramp in the right hand and were followed by a weakness of that hand. In 1922, and again in 1928, the patient had long series of attacks at intervals of a few minutes for several days. These series of attacks were associated with complete loss of power in the right arm, weakness of the right leg, and impairment of speech, and although a great deal of recovery occurred on each occasion within a few weeks, there has been some permanent weakness of the right arm since 1922. The patient now shows slight right hemiplegia with typical reflex signs, and has slight motor aphasia.

Skiagrams taken in 1922 showed a calcified ring in the region of the left Sylvian fissure. Recent skiagrams show the same appearance. The cerebrospinal fluid, examined in 1922 at a time when the patient had a long series of attacks, was normal.

Section of Dermatology

President—HENRY MACCORMAC, C.B.E., M.D.

[*March* 15, 1934, *continued*]

Multiple Plane Warts.—A. C. ROXBURGH, M.D.

G. M., male, aged 48, seen yesterday for the first time, has had asthma, bronchitis and eczema all his life. For twenty years he has had closely set papules on the inner sides of the legs; eight years ago these began to spread. Seven years ago he was seen by Dr. MacCormac, who advised repeated small doses of X-rays. These, however, he has never had. No biopsy was made at that time.

Family history.—Grandfather had asthma.

Present condition.—The whole of the body, except the face and scalp, hands, feet and neck, is covered with small, slightly domed, shiny papules, evenly distributed and not especially on either the flexor or extensor surfaces of the limbs, or in the flexures. Some of the papules are very brown, some have a mammillated surface like plane warts, especially on the back and chest, and others, especially those on the legs, are œdematous. On the front of the wrists there are papules which are obviously due to lichenification, but these appear to be different from the rest. Some of the papules on the arms rather suggest lichen planus. There is nothing in the mouth to suggest lichen planus, and there are no lichen planus scars. The eruption does not resemble that of Darier's disease, and there are no lesions suggestive of this on the sides of the neck, or in the flexures, or on the hands. The patient has some scurf on the head, and chronic eczema on the face, neck, forearms, and ankles. Most of the superficial lymph-glands are somewhat enlarged, and the nails show the high polish and concave edges characteristic of much scratching. The patient has four gold-crowned teeth.

Discussion.—The PRESIDENT said that he had seen this patient seven years ago. There was then lichenization and eczematization, and his advice was that the localized patches should be treated. His notes recorded the presence of a certain number of dome-like nodules, which he thought were nodular prurigo. On looking at them to-day he was not sure that many of them, at least, were not common warts. A microscopical examination would settle the point.

Dr. S. E. DORE said he also thought that the lesions might be warts which would be disseminated by scratching, owing to the pruritic condition present.

Dr. H. CORSI said that if the lesions were warts it would not be necessary to carry out a biopsy, as, in that case, when they were scraped with a spoon most of the material would come off. This was a good clinical differentiation between a wart and a lichen planus lesion.

Postscript.—May 3, 1934. The patient has now had four doses of X-rays ($\frac{1}{2}$ pastille) to the whole of the right leg and thigh. The eczema has considerably diminished all over the body. The papules are now all brown in colour and those on the legs are now similar to those on the trunk. They all appear to be plane warts, except the lichenified papules on the arms, which are distinct. Three papules from the upper part of the back have been excised and histological examination by Dr. Robert Klaber shows that they are, in fact, plane warts.—[A. C. R.]

Mycosis Fungoides.—GODFREY BAMBER, M.D.

Mrs. E. W., aged 66. Three months ago noticed, on the left buttock, a lump which has increased in size.

On examination a large round firm tumour, pinkish in colour, was seen on the left buttock, and in one place there were adherent crusts. To the outer side of the mass there is a scar where what the patient describes as a similar, but smaller, lump was excised ten years ago, when the patient was under the care of Dr. G. B. Dowling, who regarded the condition as lupus tumidus. She had been, and is now, in good health. The Wassermann reaction is negative.

A blood-count shows: R.B.C., 5,200,000; Hb. 98%; C.I. 0·9; W.B.C. 10,400. *Differential:* Polys. 77%; eosinos. 1%; large monos. 4%; lymphos. 18%.

Histology.—Epithelium: A slight increase in thickness, with elongation of the interpapillary processes. Slight œdema of the mucous layer; no parakeratosis.

Corium: There is a massive cellular infiltration especially in the upper third, replacing the connective tissue. This infiltrate shows extreme polymorphy characteristic of mycosis fungoides.

The tumour is undergoing X-ray treatment.

Dr. S. E. DORE said that he had had a similar case at St. Thomas's Hospital, where the original lesion was diagnosed and excised twenty years previously, and was followed by a mycosis fungoides eruption, with tumours, which proved fatal. There were said to have been no lesions of the skin in the intervening period.[1]

[*May* 17, 1934]

Cutaneous Hæmosiderotic Pigmentation from Purpura in a Woman with High Blood-Pressure.—F. PARKES WEBER, M.D.

The patient, Mrs. P. S., aged 48, was first seen by me on April 28, 1934. She is a rather fat, but fairly healthy-looking, woman, who was treated in 1932 in the hospital out-patient department for chronic arthritic swelling of both knees. Menopause about 1929. During the last four weeks before I saw her she had developed a remarkable brown pigmentation of the skin, at first of the legs and then of the thighs, and, to a lesser degree, of the front of the abdomen and the whole of the back of the trunk, but not of the front of the thorax, nor of the face. The pigmentation evidently arose from fine red purpuric (fleabite-like) spots, and there was practically no itching connected with it. Most of the pigmentation was golden-brown, but there was a darker area over the right calf, which had been observed already four weeks before the rest. There were moderate varicose veins of the lower limbs, but these could not account for the purpuric spots and pigmentation on the trunk, which was obviously mainly of purpuric origin.

Brachial blood-pressure: 225/100 mm. Hg. Nothing special by ordinary examination of the thoracic and abdominal viscera and of the urine. No enlargement of liver or spleen. Blood-count (May 12, 1934): hæmoglobin, 84%; erythrocytes, 4,600,000; leucocytes, 4,650; (basophils, 1%; eosinophils, 7%; polymorphonuclear neutrophils, 35%; lymphocytes, 49%; monocytes, 8%). Thrombocyte-count: 320,000 per c.mm. of blood. Blood-Wassermann reaction, negative. The capillary resistance (Rumpel-Leede) test, when tried on May 5, was very slightly positive.

The cutaneous pigmentation, which was apparently mainly connected with a so-called anaphylactic type of purpura (Schoenlein's purpura), was obviously clearing up when the patient was seen on May 12; the only treatment had been a little aspirin for rheumatic pains.

In appearance the cutaneous pigmentation somewhat resembled that in a man, aged 28, whose case I described in 1910, under the heading, "Chronic Purpura of Two Years' Duration Connected with Malignant Endocarditis," *Brit. Journ. Dermat.*,

[1] *Westminster Hospital Reports*, xx.

1910, xxii, p. 37. Cases of chronic purpura in endocarditis maligna *lenta* (*Streptococcus viridans*) are rare (*cf.* O. Naegeli, *Blutkrankheiten*, fifth edition, 1931, p. 426), and according to E. Frank's arrangement (in A. Schittenhelm's *Krankheiten des Blutes*, 1925, ii, pp. 461-464) fall into the class of "endotheliosis hæmorrhagica."

The slight blood-eosinophilia in the present patient is (like her purpura) probably of anaphylactic origin. The great point against the anaphylactic explanation of the case is the apparent absence of all raised erythematous elements.

It would be interesting to compare cases like the present one with cases of chronic progressive hæmosiderotic pigmentation of the skin (Schamberg's "peculiar progressive pigmentary disease of the skin").

Localized Myxœdema with Hyperthyroidism.—G. B. DOWLING, M.D.

The patient a man aged 24, has been suffering from hyperthyroidism for six or seven years. About six years ago a few small isolated elevations began to appear on the legs; these increased gradually in number and eventually became confluent forming a continuous plaque encircling the lower two-thirds of both legs. The lesions have sharply limited upper and lower borders in the immediate neighbourhood of which the skin appears to be quite normal; they are indurated, slaty-blue in colour, do not pit on pressure, and have an irregular mammillated surface. Sweating is as apparent on the affected surface as it is on the normal skin. In addition to the main areas there are groups of flat nodules on the dorsal surface of the feet, and one firm elevation on the right great toe.

The case is exactly similar to one that I showed at a meeting of the British Association of Dermatology in 1933. The patient, an elderly man, had suffered from filariasis at one time, and had had malaria, dysentery, and yellow fever at various times. He had been admitted to St. Thomas's Hospital on account of Graves' disease and underwent partial thyroidectomy there. The symptoms—palpitations, loss of weight, and exophthalmos—had been noticed only for a year, but the lesions on the leg had been gradually developing for three years.

I referred the present case to Dr. I. Muende for a pathological investigation and he has reported as follows:—

"The epidermis is unaltered. The pars papillaris of the corium shows evidence of collagen degeneration. The most prominent pathological change, however, is to be seen in the upper half of the pars reticularis, where collagen bundles exist merely as a loose network, the interstices of which are filled with mucoid substance. In the deeper parts of the corium there are numerous large phagocytes containing coarse light brown granules which prove to be blood pigment."

The problem is as to the nature of the change in the skin of the legs and its relationship to the hyperthyroidism. The hyperthyroidism began six or seven years ago, and the skin condition began to develop only a year later. Therefore it is difficult to imagine that it is a question of thyroid exhaustion. In the first case seen by me the difficulty is more apparent, for the skin changes began about two years before symptoms of hyperthyroidism were noticed.

Discussion—Dr. H. C. SEMON said that three months ago he had shown a case of symmetrical mammillated elephantiasis of the legs, in a man, aged 63. Dr. Dowling had pointed out at the time that the man had some proptosis. The pulse-rate, however, was normal, and there were no other symptoms of hyperthyroidism. In view of the patient's previous residence in Assam, he (the speaker) sent him to the Tropical School of Medicine where the test for filaria was made, but proved negative. The Wassermann reaction which, it was suggested, might throw some light on the case, was also negative. A biopsy was refused.

Dr. F. PARKES WEBER said that, though symptoms of myxœdema were exceptionally associated with late Graves' disease, patches on the legs like those in Dr. Dowling's case had apparently never been known to be associated with true myxœdema. He (Dr. Weber)

suggested therefore that these leg plaques should not be termed "localized myxœdema," but they had been observed sufficiently often in cases of Graves' disease to make a causal connexion with hyperthyroidism extremely probable.

Dr. J. M. H. MACLEOD considered that the name myxœdema of the skin was inappropriate. He had examined sections from this case and found a mucin degeneration of the affected corium which was the result of basophilic degeneration of the collagen and elastin. It was not the type of skin that occurred in myxœdema and it would be more appropriate to designate the condition as a mucoid degeneration of the skin associated with hyperthyroidism.

Dr. I. MUENDE said he had examined the skin of this case still further to find out whether it corresponded with Unna's description. He stained particularly for the degeneration products of collagen and elastin and his first results showed that this condition was associated with the development of both elacin and collastin, thus showing the changes which Unna described. He was continuing his investigation to determine the origin of the blood pigment, a large amount of which was free in the corium.

Dr. DOWLING (in reply) said he agreed with Dr. Parkes Weber and Dr. MacLeod that the name should be altered; he used the term "localized myxœdema" only because this appeared to be the official name for the condition. He never regarded it as a localized myxœdema in the true sense of the term.

Two Cases of Rosaceous Tuberculide.—H. W. BARBER, M.B.

Lewandowsky[1] has described a tuberculide eruption of the face, which simulates rosacea, and I am showing these two cases because although in my experience not very uncommon, the condition is usually wrongly diagnosed even by expert dermatologists, as ordinary rosacea, with secondary papulo-pustular lesions.

Case I.—Mrs. N. P., aged 27.—The eruption first appeared in May 1932, about two months after she ceased to suckle her only child. She consulted a dermatologist who gave her instructions as to diet, some internal treatment, and sulphur applications locally. A point of importance is that the lesions were uninfluenced by the sulphur.

She came to me on January 16, 1934. At that time she had very severe rosacea with large numbers of papules, some of which were capped by necrotic pustules. On careful examination of the non-pustular papules, one could recognize that they differed from the inflammatory papules which complicate ordinary rosacea. They were less red, being either lupoid or bluish in colour, and somewhat translucent. On vitropressure the lupoid appearance was enhanced. Apart from the clinical features of eruption, the following points seemed to me of importance :—

(1) The patient had had no acne as a girl. (2) She had no indigestion. This, of course, is also true of some cases of true rosacea. (3) Neither the local nor internal treatment, given her on the supposition that she had rosacea, had the slightest effect. She stated that she was losing weight and became unduly tired on exertion.

Skiagram of chest.—"Median opacity normal. Diaphragms move evenly and well. Costo phrenic angles clear. Large dense roots with glands. A few small foci below at right apex (? old).

Tuberculin tests.—(Mantoux) one-in-five-thousand, negative ; one-in-five-hundred, definitely positive, both to human and bovine tuberculin.

A generous dietary, rich in vitamins and calcium, was given, with radiomalt, and syr. calcii lactophosph. B.P. Injections of solganal B were begun on February 5, 1934, and so far the patient has had eleven injections.

The result of this line of treatment has been very striking. Pustulation has almost ceased, many of the papules having disappeared, leaving small pitted scars, and the flushing of the face, which was at first very obvious, has markedly diminished.

[1] Lewandowsky, F., *Cor.-Bl. f. schweiz. Aerzte*, 1917, xlvii, 1280.

Case II.—Nurse C. W., aged 46, consulted me on March 13, 1934. The eruption had been present for eighteen months, and had been diagnosed as ordinary rosacea by a dermatologist whom she had previously seen. In this case, however, the diagnosis of rosaceous tuberculide was more obvious than in Case I. The eruption involves not only the rosaceous area, but also the temples and the forehead near the margin of the hair. There is much less tendency to pustulation than in Case I, and the papules are more clearly lupoid in character. This is well seen on vitropressure on the temples and forehead.

Skiagram of chest.—"Median opacity normal. Diaphragm moves evenly and freely. Costo-phrenic angles clear. Large dense fibrotic roots with old dense foci here. Interlobar streak on right."

Tuberculin tests.—(Mantoux) 1:5,000 human tuberculin, slightly positive; 1:500 human tuberculin, markedly positive; 1:500 bovine tuberculin, slightly positive.

The same line of treatment has been instituted as in Case 1, but it is too early yet to judge of its effect.

Discussion.—Dr. J. E. M. WIGLEY said he did not feel convinced by the evidence as to the tuberculous nature of the lesions in these cases. All dermatologists had experience of cases of ordinary rosacea which failed to respond to treatment, and the improvement of any condition under gold-therapy could hardly be taken as evidence of its tuberculous nature. The skiagrams of the chest showed shadows consistent with *healed* tuberculous lesions, which would be present in a very large number of apparently "normal" adults, as would the positive Mantoux and Pirquet reactions. Perhaps Dr. Barber would be good enough to show histological sections of the lesions, and also to show these patients in six months' time so that their continued improvement under his treatment could be observed.

Mr. TWISTON DAVIES said he had recently seen two typical cases of rosacea mistaken for lupus erythematosus and treated with injections of krysolgan with remarkably good immediate result.

Dr. BARBER (in reply) said that he made a point about the appearance of the papules which were different from those complicating ordinary rosacea, especially in the second case. He would, however, try to obtain a biopsy in that case, and, to convince members, he would show the case again. There was a good photograph of the condition in Schaumann's article on the tuberculides.

ADDENDUM (25.7.34). A biopsy was made from a group of lesions on the forehead in Case II, and serial sections were cut. Microscopical examination showed an intact epidermis, and in the dermis were fairly well-defined areas of cellular infiltration, composed of epithelioid cells, lymphocytes, and occasional giant-cells.

[H. W. B.]

Acne Agminata.—H. SEMON, M.D.

Miss E. R., aged 21, for the past eighteen months has suffered from a recurrent eruption limited to the right half of the face. The skin has been irritable and redder at some times than others. The symptom is not aggravated by meals or other factors and there is no dyspepsia or constipation. The teeth are in good condition, and there is no history of sore throat suggesting a septic focus in the tonsils which are not enlarged. Treatment by her doctor with ointments, lotions, and ultra-violet rays effected no appreciable improvement.

Past history.—No history of pleurisy or glandular trouble.

Family history.—Mother suffers from asthma. Father is stated to have had hæmoptysis on two occasions at the age of 32, but tubercle bacilli were never found in the sputum, and he is alive and well to-day.

General health.—The patient is a slender and rather delicate-looking subject. The physical examination did not reveal clinical evidence of tuberculosis in the lungs and a skiagram of the chest proved negative. Tuberculin, T.A.F., intradermally,

0·0001 c.c., was positive and when repeated elicited a positive track reaction with a temperature of 99° F. T.A.F. 0·001 c.c. produced a temperature of 101·4° F. and irregular mild pyrexia with a strong track reaction for five days. Subsequent treatment with bacillary emulsion (B.E.) has produced a fine scaling on both cheeks and the patient states that the eruption has since become more apparent on the left cheek on which previously it was scarcely noticeable. The physical signs include a slight chronic erythema, mostly on the right cheek and very small erythematous papules, among which minute pustules can be seen with a lens. This also reveals minute pitted scars of old lesions. There are no comedones, and there is no excessive scurf in the scalp or anything suggestive of a seborrhœic tendency.

The case does not conform to the typical appearances of well-developed acnitis (Barthelemy), or acne agminata (Crocker) and diascopy does not reveal the brownish infiltration characteristic of the tuberculous papule or pustule. Nevertheless I think that, for the reasons given above, ordinary acne vulgaris can be excluded, and in view of the striking effect of tuberculin a tuberculous ætiology seems probable.

Sarcoid of Boeck.—HUGH GORDON, M.R.C.P.

This patient, a woman aged 26, gives a history of attacks of erythema nodosum extending over a period of six years. She has had, in all, four attacks, the last of which occurred in June 1933. These were seen by various doctors, and her description of them bears out the diagnosis.

The present eruption began in September 1933, on the shins, and has since spread to the thighs, and also, slightly, to the upper arms. The lesions, when they first appeared, were bluish, intracutaneous nodules, such as those now present on the top of the thighs. On the shins, where the oldest lesions are present, are now seen groups of yellowish-brown pigmented nodules, which are well defined, and remain on glass pressure.

Dr. Hern had found no evidence of tuberculosis anywhere in the system. There was no enlargement of the spleen, and there were no physical signs in the chest. There is definite glandular enlargement, both epitrochlear glands being palpable, and there is a history of swollen glands in the neck in childhood.

In appearance the patient is particularly robust. X-ray examination shows a distinct fine mottling of the lungs; no fibrocystic changes in the bones of the hands are discernible.

Wassermann reaction, negative; Mantoux reaction, negative.

Report on section (*Dr. R. Klaber*).—Epithelium: Normal. Corium: Scattered through all layers are several compact, well-defined, irregularly shaped masses of epithelioid cells, with very few lymphocytes on the borders. There is an occasional attempt at giant-cell formation and a suggestion of early diffuse degeneration in these masses. Examination of an earlier nodule shows rather more marked degeneration, indicated by karyorrhexis and poor staining of the cells constituting the masses. An occasional giant-cell of Touton type is seen in serial sections, and lymphocytes are slightly more numerous. The lesions, however, do not show any of the giant-cell systems indicative of tuberculosis. Examination of serial sections stained by Ziehl-Neelsen has shown no tubercle bacilli.

Opinion.—The occurrence of occasional giant-cells and slight necrosis in these masses, though absent in Boeck's original description of sarcoid, has been previously described by Kyrle, and also by Kissmeyer, as an occasional feature of its histology.

This case is of interest in demonstrating the association between erythema nodosum and sarcoid. Goekerman, in "Archives of Dermatology," in 1928, reviewed a series of 17 cases of sarcoid. His general conclusion was that the so-called sarcoid of Boeck, the sarcoid of Darier-Roussy, lupus pernio, and erythema induratum, are so closely related, both histologically and clinically, that a sharp dividing line can only with difficulty be drawn between any two of them. He supports the theory that they are all of tuberculous origin in subjects who are anergic,

and are possibly skin reactions to dead bacilli. In his group of cases, four were found to have diffuse, fine mottling of the lungs, which he supposed to be due to infiltration of the finer bronchials. In one of his cases, an eruption on the legs, resembling erythema nodosum, occurred, together with a plaque on the face, clinically resembling sarcoid of Boeck.

In the present case, the clinical appearances are by no means typical of the sarcoid of Boeck, though the biopsy fully confirms the diagnosis.

Dr. J. M. H. MACLEOD said he thought that the description of the histology was strongly suggestive of sarcoid. At the present time he had under his care a case of sarcoid of Boeck, in which an extensive sarcoid eruption was associated with tuberculous ulcers on the leg. A biopsy had been made of one ulcer and tubercle bacilli were found in a section.

Peculiar Urticaria.—HUGH GORDON, M.R.C.P.

This case has been entitled "urticaria," for want of a better name.

The patient, a youth aged 18, has found, for the last five years, that streaks appear on the skin at points of pressure, or even on scratching. These streaks are, in fact, exudation of blood, and pigmented marks appear which remain from two days to two weeks. The marks at present visible on his chest were produced by himself by scratching last night.

True dermatographism is present in only a very slight degree. There are no subjective symptoms.

Wassermann reaction, negative; blood-calcium, normal; bleeding-time prolonged. History of excessive nose-bleeding. There is no familial history.

Mycosis Fungoides treated by Malaria.—H. MACCORMAC, C.B.E., M.D. (President).

B.S., aged 48, was first seen in 1931 with an eczematous eruption on the face, trunk, and limbs which at first improved under local treatment, subsequently relapsing and becoming unexpectedly resistant to all the ordinary applications. No suspicion of the true nature of the disease was entertained until March 1933, when infiltrated plaques, typical of mycosis fungoides, developed and extended over the trunk and limbs, mixed with eczematous areas. Later, definite tumours appeared which at first responded to X-ray treatment. Apart from an eosinophilia, the blood picture exhibited no unusual features. In course of time the disease gained ground and became too extensive and too rapid in its development to be controlled by radiotherapy. About this time I was discussing with Dr. Gordon the effects of intercurrent erysipelas on mycosis fungoides, and malaria therapy as a possible alternative. It was decided to treat the patient in this way and the Ministry of Health kindly put at my disposal the means of injecting the patient. A direct inoculation was made on April 4, the patient subsequently developing fever which reached 105° F. and was allowed to continue for nine days. The result of this treatment has been remarkable. The tumours rapidly flattened and almost entirely disappeared and it was hoped that a permanent result had been obtained. The improvement has not been completely maintained; nevertheless the aspect of the case has been entirely modified for the better.

The experiment, although incomplete, serves to indicate a line of treatment from which promising results may be obtained when its application has been more fully investigated.

Discussion.—Dr. A. M. H. GRAY said he was interested in a question raised by this case. He did not know whether what had occurred was attributed to the rise of temperature or to specific infection by the malaria parasite. He had at present in hospital a patient who had extensive mycosis fungoides. He developed severe erysipelas which lasted nearly a fortnight, and the effect was to bring on the disease with renewed virulence. There was not even temporary improvement, except in the areas actually the site of the erysipelas.

The PRESIDENT (in reply) said that he had used malaria-therapy in mycosis fungoides as a form of febrile reaction which was safe and could be controlled. No doubt other factors than the febrile reaction were concerned; nevertheless he believed that a continued febrile process was essential, in fact, something similar to the reaction occurring in intercurrent erysipelas.

The beneficial effects of erysipelas in two cases of mycosis fungoides, as recorded by him, had led up to the present experiment, and although one of the patients had since died, the other remained relatively free, twelve years having elapsed since the attack of erysipelas.

? Xerodermia Pigmentosa.—C. H. WHITTLE, M.D.

M.S., a female infant, aged 1 year and 11 months.

One year's history. The lesion was preceded by an attack of eczema of the face. After this had subsided a patch of brown pigmentation appeared under the left eye and spread over the cheek, extending to the right cheek and chin.

The lesion has a fairly sharp edge and consists of a network of dilated blood-vessels in the skin, not raised, with slight pigmentation, and a slight tendency to scaling and superficial atrophy or scarring. Between the meshes of the network, which are about $\frac{1}{4}$ in. wide, the skin is of normal or slightly pale colour.

The child appears to be well but is backward, there being only about half the teeth erupted, and the weight being below normal (21 lb.). Also the hair is scanty.

The family history is interesting, in that the mother and father are first cousins, but there is no evidence of other members having been similarly affected. The patient is an only child.

Ahlswede, in his textbook, mentions inbreeding as an important ætiological factor. ("Practical Treatment of Skin Diseases," 1933.)

Dr. WIGLEY said he thought the condition was really a variety of nævus, comparable to the nævus araneus. He suggested trying the effect of painting the area with carbon dioxide snow dissolved in acetone.

[*The report of other cases shown at this meeting will be published in the next issue of the* PROCEEDINGS *of the Section.*]

Section of Otology and Section of Laryngology

COMBINED MEETING

HELD AT BIRMINGHAM, JUNE 8 AND 9, 1934

[*June* 8, 1934]

DISCUSSION ON THE OPERATIVE TREATMENT OF FACIAL PALSY

Chairman—W. J. HARRISON, M.B. (President of the Section of Otology).

The Operative Treatment of Facial Palsy: with Observations on the prepared Nerve-Graft and on Facial Spasm.

By Sir CHARLES BALLANCE, K.C.M.G., M.S.

THE earliest experiments (1827) on the suture of nerves were those of Flourens.[1] It appears that as the result of an experiment, a part of the central nervous system had to relearn its function, for nerve-fibres previously conveying impulses to extensor muscles subsequently carried impulses to a flexor group of muscles and vice versa.

Since the year 1895 surgeons have been uniting the peripheral end of the divided facial nerve to the central end of some other divided nerve of the neck. The recovery of the muscles of the face after such an operation, though often wonderfully satisfactory as compared with the preceding paralysis, was never functionally perfect. To witness the slow restoration of the function of the muscles of the face was such a wonderful experience that surgeons, to speak for myself, were apt at first to ignore certain disabilities associated with these operations.

After the conclusion of the Great War I determined to investigate by the experimental method the question of the best method of operation for facial palsy. Thirty experiments were carried out in which the facial nerve was united to various nerves of the neck. Mr. Lionel Colledge helped me in many of the experiments. At the end of six or seven months, voluntary movement and faradic response were normal in several of the animals. At any rate, scarcely any difference could be detected on comparing the movements and electrical response of the muscles of the two sides of the face. Further, the muscles on both sides of the face contracted together. Nevertheless, when the facial nerve was grafted to the hypoglossal nerve, the descendens hypoglossi nerve, or the glossopharyngeal nerve, associated movements varying from slight closure of the eyelids to contractions involving other muscles of the face and pinna were present.

Such was the stage of the facial palsy problem when I received a long cable from Dr. Arthur Duel of New York (March 1930) inviting me to carry on surgical research in that country. At Laurelwood, Dr. Duel's country home, eighty miles from New York, in his own surgical laboratory, we commenced again to attack the problem of the operative treatment of facial palsy. We did not arrive at the decision to employ a nerve graft in the Fallopian canal by a sudden inspiration. The method was conceived slowly, after nearly a year of experimentation.

[1] "Recherches expérimentales sur les propriétés et les fonctions du système nerveux, dans les animaux vertébrés." Edit. Paris. J. B. Baillière, 1842, p. 272.

Some of the experiments were not directly associated with the problem of the cure of facial palsy. For example, those on Louisiana frogs were related to the conduct and fate of nerve-grafts. From all the experiments there was something to learn of value concerning the surgical problem on which we were engaged. The natural sciences are so closely linked together that the investigation of one sheds light on the others.

Before proceeding further, let me point out that there is in the so-called anastomosis operation no such thing as the anastomosis of nerves. The distal segment of the nerve degenerates. In this state it may be described, say at the end of fourteen days, as a bundle of tubes containing the broken-down fatty elements of the nerve-sheath. The axis cylinders of the central segment of the nerve slide along the tunnels, pushing aside the lipoid masses, till they reach the motor end-organs of the muscle or muscles which had been in connexion with the fibres of the original distal segment. The new fibres thus replace the old and carry the nerve impulses which cause again contraction of muscle-fibre.

The decision to form an intratemporal operation for the cure of facial palsy was strengthened by the consideration that the fundamental principles of surgery demand that an injured nerve, like a wounded artery, should be exposed at the site of injury. In all parts of the body, except where the injured nerve lies in the aqueduct, it is exposed at the site of injury. There is no reason why an exception to a fundamental rule should be allowed.

In man, the complete or radical mastoid operation should be done before the removal of the outer wall of the aqueduct is commenced. When the nerve is injured in the aqueduct during an operation, or when palsy occurs, during the course of acute or chronic otitis, the appropriate operation should be performed at once. Decompression is the obvious treatment to adopt. The facial nerve should be exposed for 4 or 5 mm. above and below the site of injury or disease. In many cases the best plan is to expose the nerve from the geniculate ganglion to the stylomastoid foramen. In patients a surprising length of damaged nerve has had to be removed, and to fill the gap often requires a 10 mm., 15 mm., or even a longer graft.

Alt performed decompression in 1908 and his case is a model for all to reflect on.[1] He relates an instance in which, on operating on account of cholesteatoma in a woman aged 32, who had complete facial palsy before operation, he found an opening 3 mm. long in the facial canal. He exposed the nerve for some distance above and below this defect, turned it out of the canal, cleansed it by wiping and replaced it in the groove. In seven months the recovery was complete. The important point emerging from Alt's case is that excision of the damaged portion of the nerve and the use of a nerve-graft are not always necessary. The decision of this difficult problem depends on the experience and judgment of the surgeon.

In certain cases of palsy from inflammation of the geniculate ganglion and in certain cases of palsy due to exposure to cold, in which the sheath of the nerve in the vertical portion of the canal becomes inflamed, decompression is the ideal treatment. The outer wall of the aqueduct is removed and, with the utmost care, the sheath of the nerve is slit up.

Dr. Duel and I are not in favour of the type of operation which aims at shortening the course of the nerve by displacing it from the canal. The shortening thus gained is at best 3 mm. The nerve lies across the inner wall of the tympanum. The new bed cannot compare with the old and the vascular connexions in the aqueduct are broken.

The mastoid wound at the close of the operation is not stitched. It is kept widely open. When an accurate length of graft has been inveigled into the aqueduct no suture is required. The graft soon becomes fixed, owing to the coagulation of plasma or by clotting of blood. Dr. Duel and I have usually covered the graft and the exposed nerve for a few days by gold-leaf or gold-foil, so that there should be no chance of drag on the graft region during the renewal of the dressings. The dressing consists of sterilized ribbon gauze moistened with sterilized salt lotion, and it is changed daily.

[1] Alt, F., *Verhandl. d. deutsch. Otol. Gesellsch.*, 1908, xvii, 191.

The way in which the brain cortex reassumes control of the facial muscles is best understood by the study of other cases in which the conditions present are somewhat comparable to facial palsy after a remedial operation has been carried out. When the speech centres of the left side of the brain are destroyed in early life the power of speech usually returns. We assume that the dormant centres on the right side of the brain acquire the function that would otherwise belong to the centres of the left cerebral cortex. Here is an illustration of the education of a new centre in the brain for the performance of a function after the usual centre is destroyed.[1] Is such a case exactly comparable to one of facial palsy for which a remedial operation has been performed? Do the cells in the facial area of the opposite Rolandic cortex atrophy and become no longer of any service in the case, say, of facial palsy of six months standing? One can only report that in none of our baboons was there any evidence (by electrical stimulation) that the centre of the opposite cortex had acquired the function of the usual centre. It should be remembered that in the baboons the facial palsy dated from the time of the experimental operation.

The expression of the emotions is the best test as to whether the operation has been followed by the harmonious working of the two sides of the face. In the baboon the expression of the emotions such as surprise, fear, anger, remind one of the expression of similar emotions in man, but in the face of the baboon the finest lines of emotional expression are absent. In winking and yawning, and in anger it is clear that in many of our animals the two cerebral hemispheres are working in unison. The two great motor systems, the neokinetic and paleokinetic, have both a functional representation in muscular movements. The paleokinetic and paleostatic systems subserve the function of the automatic-associated movements and postures. The early stages of the muscular recovery in facial palsy are in functional relation to the paleo-encephalon. It is only later, when voluntary movement and emotional expression are visible in the face of the baboon, that it becomes clear that the neopallium is taking its part in the recovery of the previously paralysed muscles.

The use of nerve-grafts.—Before I left America Dr. Duel and I had carried out on baboons and rhesus monkeys a long series of experiments in which a portion of the facial nerve in the Fallopian aqueduct was replaced by a fresh nerve-graft. The results of the experiments proved this method to be far superior to the suture of the peripheral end of the divided facial nerve to the central end of some other divided nerve of the neck, in regard to the speed and completeness of recovery of the palsied muscles, and to the absence of associated movements.

But we had the opportunity not only of watching the recovery of the muscles of the face in animals in which the nerve-graft operation had been performed but also of studying the recovery of the face muscles in patients on whom Dr. Duel had carried out the nerve-graft operation.

The next stage in progress is one for which Dr. Duel is in a true sense responsible, i.e. the employment of degenerated grafts instead of fresh grafts. I was unable to continue this particular part of the research at the Royal College of Surgeons because there are no baboons there. This however is of no consequence, for Dr. Duel with wonderful energy and enthusiasm has splendidly demonstrated on numerous monkeys and many patients the surgical value of degenerated grafts.

A degenerated or prepared graft consists of a series of tubes filled with fatty masses due to the breaking up of the sheaths. Through these empty tunnels the axis cylinders slide along, as Dr. Duel tells me, with shocking facility. Cajal was the first to foretell the practical value of the degenerated graft. He writes:

"The ideal graft is the peripheral stump, with bands of Büngner newly taken from an operated animal eight to fifteen days after the operation. (The bands of Büngner are the phase of longitudinal striation, which appears during the degeneration process.) The newly

1 Spiller, *Univ. Penn. Med. Bull.*, Nov., 1903, xvi, 306.

formed fibres travel through the empty sheaths with extraordinary speed, deviations and retrogressions being much diminished."[1]

It would seem that Cajal was led to recommend the use of degenerated grafts by the experimental work of Tello, who implanted portions of the sciatic nerve into the cerebral substance.[2] Fresh grafts were absorbed while degenerated grafts attracted the nerve-fibres of the brain. These penetrated the open ends of the prepared grafts. Tello states that

"The empty channels of the degenerated grafts are especially rich in neurotropic substances, whereas in the normal nerve grafted directly, though not entirely absent, they are liberated very tardily."[3]

When I tell you that the use of a degenerated graft may determine the return of faradic excitability in the muscles of the palsied face in the short period of one month, you will agree that a notable advance in the treatment of facial palsy has been made. It is of great importance to appreciate the fact that the earlier the operation is performed, the more perfect will be the recovery. The fresh nerve-graft is abolished from surgical practice. Whenever and wherever a nerve-graft is required in surgery a degenerated graft should be employed.

A fresh nerve-graft placed in the aqueduct of Fallopius degenerates in the same manner as if it had been left attached to the peripheral segment of a divided nerve, say for two weeks. In such an experiment it would seem at first sight that the use of a fresh nerve-graft would delay the recovery of the paralysed muscles for only two weeks. But this is not so. A long delay occurs, as compared with what happens when a degenerated graft is inveigled into the aqueduct. Why is this? In the first place, a fresh graft is not in an anatomical or physiological state favourable for the passage of axons. Secondly, the fresh graft is a foreign body, which becomes surrounded in two weeks by young fibrous tissue which blocks the ends of the graft, thus forming a barrier to the immediate entrance of axis cylinders. Deviations and retrogressions of the axons take place, and much time is required before they are able to pierce the cork of young fibrous tissue, whereas the axis cylinders can and do enter at once the freshened ends of a prepared graft.

Spontaneous contraction of the muscles of the face in man and baboons.—In 13 of our first series of 22 experiments on baboons, Dr. Duel and I observed spontaneous contractions of the muscles of the face. In eight of the 13 experiments the facial nerve had been grafted to another nerve of the neck. In the remaining five experiments the nerve-graft operation in the aqueduct had been performed.

The spontaneous contractions of the muscles of the face in the baboons are exactly comparable to those that occur in man when the recovery of the paralysis of the face is long delayed and is more or less imperfect. They are the common and permanent result of long-continued medical treatment. Often some muscles remain paralysed, others offer a poor response to faradic stimulation, and still others, notably those around the angle of the mouth, are the victims of spontaneous twitch which has been described as the "winking reflex." The twitch may be rhythmical in time and continuously present, or there may be intervals of quiescence between the rhythmical spasms. The twitch may be only elicited by stroking the eyelids or face. If present, stroking the eyelids increases the spasm. Excitement or fear is the cause of wider excursions of the muscular contractions. It is noteworthy how frequently the risorius muscle is involved in spasm, and this may be so even when no response can be elicited in the muscle to the faradic current applied through the skin.

1 "Degeneration and Regeneration of the Nervous System": translated by Raoul May, 1928, i, 361.

2 "Cajal, ibid, ii, 741.

3 Tello, "La influencia del neurotropismo en la regeneración de los centros nerviosos," *Trab. del Lab. de Investig. Biol.*, 1911, ix, 123.

Light anæsthesia may produce the twitch when, during ordinary life, there is no twitch. Anæsthesia cuts out the control of the neopallium.

"The spasmodic manifestations in the kinetic sphere occur as the result of irritation, or as release phenomena in subordinate motor systems due to loss of higher inhibitory control." [1]

If the cerebrum is removed by section of the crura cerebri, the carotid arteries being clamped to avoid hæmorrhage, the spasms of the facial muscles become still more exaggerated; the monkey continues to breathe and live on its brain-stem. This experiment demonstrates that "the paleo-encephalon, represented by the corpus striatum and optic thalamus, which constitute the higher co-ordinating sensory and motor mechanisms of the lower forms of life," has, like the neo-encephalon, some control over the facial spasms, and therefore the removal of the paleo-encephalon is associated with wider and more marked muscular spasm.

We now come to the study of "the segmental nervous system which contains the reflex systems of the neuro-axis, and is the archaic representation in man of the nervous reactions of the lowest forms of life" for the explanation of the spontaneous muscular contractions.

We know that section of the trunk of the facial nerve is associated with regressive changes in the pyramid cells of the facial area of the opposite Rolandic cortex. Are there also regressive changes in the cells of the facial nucleus in the medulla? I am able to demonstrate to you that such changes do occur. I believe that they are the essential cause of the muscular spasms of the face which I have observed in man and monkeys. The spasms are really local epileptic phenomena which are caused by disorder of cell function. They are never the result of obstruction to the passage of nerve impulses travelling along nerve-fibres.

A localized epileptic spasm may be due to various causes. I remember a case in which I performed a craniectomy in the expectation of exposing a cerebral tumour. There was no tumour to be seen, but there was a small scar on the cortex cerebri. I watched the cortex. The brain around the scar became alternately pale and rose-coloured. The vascular disturbance in the region of the damaged cells of the cortex was the cause of the local spasm.

What happens when there are degenerative changes in the cells of the medullary facial nucleus? Around a degenerating cell, tissue and vascular changes occur. A living and active cell requires more blood than a sick cell. We must look to the disorder of the cells of the facial nucleus, surrounded as they are by vascular changes, for the essential cause of the local spasm of the face muscles.

Neither Dr. Duel nor I have observed, after operations on patients with paralysis of the face, any spasm of the muscles, yet as already mentioned, in 13 out of 22 experimental operations, the animals exhibited this symptom. Wherein lies the difference in this respect between man and monkey?

In the baboon, the facial palsy is recent. It dates from the time of operation. With the section of the facial nerve, the cells of the facial area of the opposite Rolandic cortex and the cells of the facial nucleus in the medulla commence to degenerate. The degeneration process ceases at any rate in the cells of the cortex if the operation is followed by the passing of nutritional impulses within a reasonable time to the paralysed muscles. The cells slowly regenerate. During all the time of degeneration and of regeneration the cells are in a state of physiological disorder. They are in unstable equilibrium. This, I believe, is the explanation of the spasm symptom.

Now compare the condition of the facial medullary nucleus of a patient with facial palsy with that of the cells of the facial nucleus of one of our experimental animals. In man, the operation for the cure of facial palsy is often delayed for

[1] Ramsay Hunt, "The dual nature of the efferent nervous system," *Arch. Neur. Psych.*, 1923, x, 37, and other papers.

many months, or even years, in the vain hope of recovery from the palsy without operation. The cells of the facial medullary nucleus are atrophied. Tissue and vascular activity are in a state of stable equilibrium. There are no degenerating processes going on and no associated vascular changes proceeding. This appears to be an ample explanation of the fact that in man facial spasm following a remedial operation is not observed. If Dr. Duel and I had severed the trunk of the facial nerve in a baboon and allowed the face to remain paralysed for, say six months before the curative operation was carried out, it is probable that in this experiment muscular recovery would have been recorded without facial spasm.

The twitch or spasm has a periodicity or rhythm. Though respiration is the best example of rhythmic action, it is not improbable that all living processes are more or less rhythmic in action. "The respiratory centre is capable of beating with its own inherent rhythm. Its cells are not simply passive agents only controlled by afferent messages."[1] The muscular spasms described above may be looked upon as due to an arrhythmia of cerebral cell activity.

Experiences with Fascia Lata Grafts in the Operative Treatment of Facial Paralysis.

By Sir HAROLD GILLIES, C.B.E., F.R.C.S.

Objects of the operation.—This type of operation must not be confused with nerve-grafting, which one hopes will eventually become so successful that few, if any, cases of paralysis will remain uncured.

It is essentially a palliative operation and, like a cock-up splint to a cut musculo-spiral, it serves as an internal grafted surgical splint to counteract the overaction of the opposing muscles. In addition to this surgical stay effect the loops of fascia are now attached to muscles other than the facial, such as the temporal and masseter; and when these muscles are voluntarily contracted a movement simulating facial expression is produced. Emotional response is, of course, out of the question unless an intensive training is ever found to produce an associated movement.

Points of interest in a résumé of previous work.—The use of transplanted fascia lata has now had a sufficiently extensive trial in other conditions to prove its worth as a means of support in facial paralysis. The experimental work of Gallie and Le Mesurier [1] first established it as a reliable method of cure of extensive herniæ and for their purpose the fascia was obtained in strips through a long incision in the thigh. The method of obtaining the fascia was later modified by Masson of the Mayo Clinic and others who used a more convenient form of ring-stripper and cutter necessitating only a tiny incision in the leg, and thus avoiding a long and unsightly scar.

Blair [2], New, Wardill [3], Brooke [4], Lodge [5], Fischer [6], Sheehan [7], and Moskowicz [8], have all recorded their experiences with the type of operation in which fascia lata bands form a fixed support. The improvement in facial symmetry is marked, and subjectively the patient is usually much more comfortable. No movement on the paralysed side is developed, though not infrequently the amount of recovery which sometimes occurs is hastened by the support given to the paralysed muscles. In the second method a certain degree of support and, in addition, muscular movements are obtained by means of the transplantation of the muscles of mastication into the paralysed parts. The temporal muscle, with or without the addition of the masseter, is split into segments; each with a nerve supply, and is implanted into suitable positions. The manœuvre, as described by Eden [10], Gillies [11] and by Lexer [9] and Rosenthal, has been favourably reported on by Halle [13] and

[1] E. D. Adrian. *Journ. Physiol.*, 1933, lxxix, 347, 356.

Sheehan. A definite objection to this operation is that the support is unsatisfactory. The third method, for which some originality may be claimed, is a combination of support by means of fascial slings, and muscular movement by transplantation of temporal muscle in such a way as to create a new muscle acting from the temporal region and having as its tendon attached to the angle of the mouth a band of fascia lata. The present communication records several encouraging examples of this manœuvre.

Method of taking the grafts.—There are two main methods of taking the graft: (1) the open method, and (2) the closed.

The open method, as is well known, consists of making a long incision to expose the fascia lata on the outer aspect of the thigh. The closed method consists of making a small incision above the knee, exposing the fascia, and using the ring-stripper and fascia cutter. In some clinics this method is barred because on one occasion hernia of the vastus externus was said to have interfered permanently with the use of the limb. The writer has not found this to be a serious risk in his experience.

Methods of application.—The loops of fascia lata are usually passed round the facial muscles at one or more of the following points: (*a*) the centre of the lower lip; (*b*) the corner of the mouth; (*c*) the centre of the upper lip; (*d*) round the palpebral fissure (fig. 1, p. 100). The most convenient instrument for passing these loops round the muscles is the Blair type fascia needle. It can be operated through tiny incisions in the situations named. It is considered advisable to embrace the fibres of the non-paralysed muscle in the upper and lower lip. The first series of cases had separate loops to each spot and these were fixed to the fascia in front of the ear. This hold seldom gives; but the hold given by the loop round the paralysed circumoral muscle at the corner of the mouth usually does give and has subsequently to be tightened. As the paralysed half of each lip is much elongated, these loops are used to prevent this attenuation, in addition to acting as a general stay. To effect this a loop must be passed from the corner of the mouth to the centre of each lip (fig. 2). A convenient method of applying this particular support is to pass a figure-of-8 loop embracing both upper and lower paralysed muscles and fixing the same at the corner. From the corner another loop or possibly a continuation of the same can be taken up to the point of fixation. In later cases the point of fixation was round the zygoma, still later to the fascia over the temporal muscle, the band passing deep to the zygoma, the idea of this variation being to pull the corner of the mouth upwards and backwards and so produce a more normal appearance. The fascial bands are attached to their fixed point by means of either silk or catgut sutures. The writer prefers catgut. In addition if a loop has been passed round the upper or lower lip, or both, to prevent their over-elongation, that loop must be fixed by sutures.

Activation of the face by attachment of fascia lata to temporal-muscle flap.—Activation of the facial muscles is now considered advisable and possible by attaching a flap of the temporal muscle to the band and loop in such a way that when the temporal muscle is contracted voluntarily by the patient a movement of the face occurs simulating facial expression (fig. 3). It was wondered whether an individual patient would learn by practice to associate mentally the temporal muscle action with that of the facial. To a certain extent one of the patients has learnt to do this, but it was felt that, if caught unawares, the patient's control would break down and the previously exhibited semi-response to emotional stimulus would no longer be demonstrated.

In a War case, in 1917, the writer brought down the temporal muscle-flap to fill in the gap caused by the loss of the malar bone and to simulate expression in this neighbourhood and assist in the closure of the eyelids [11].

It is obvious—as in the cases shown—that if a flap of temporal muscle is detached from its origin and turned downwards and forwards over the zygoma, there

will be a considerable bulge in this neighbourhood. Sheehan therefore advocates the formation of a channel in the zygoma to accommodate the muscle belly. The writer has not done this. The muscle belly is prepared and isolated, its nerve supply being kept intact. It is freed from the superficial layer of the temporal fascia which is attached to the zygoma, but the deep layer which forms the sheath of the muscle is kept intact. A band of fascia lata is now spread over the raw

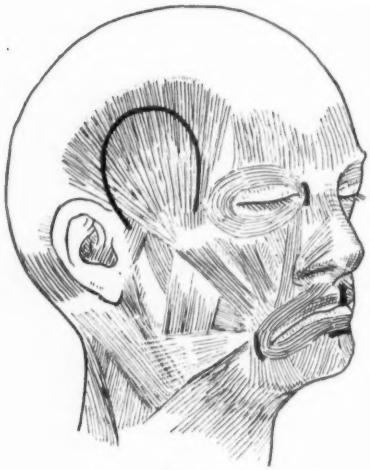

FIG. 1.

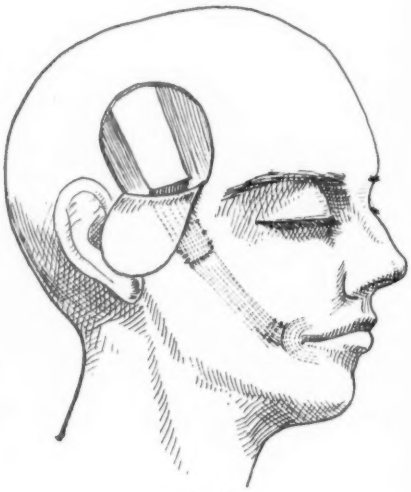

FIG. 3.

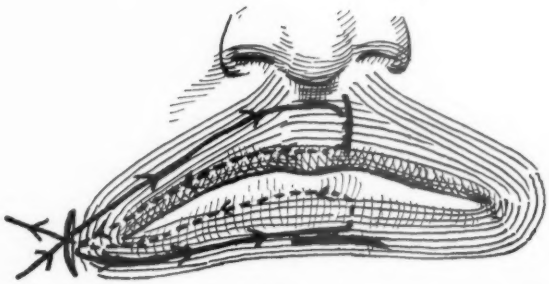

FIG. 2.

surface of the muscle, viz., that surface opposite the one covered by the deep temporal fascia, and is sutured into this position. The muscle belly is therefore encircled with a fascial sheath with a continuation of pseudo-tendon of considerable length. The fascia needle is now passed through the incision previously made at the corner of the mouth and, when drawn down, the muscle belly is pulled into the pre-zygomatic pocket which has been prepared for it. It now remains to attach this pseudo-tendon to the stay loop which encircles the paralysed circumoral

muscle at such a tension that will give a straight mouth and nose at rest, and a simulation of expression when the temporal muscle is contracted.

Treatment of the paralysed eyelid.—During the Great War many experimental operations were attempted by the author in the form of spring cartilages to encircle the palpebral fissure with not very practical results [12]. Fascial loops encircling the fissure have been passed and fixed at one or other of the canthi. A fascial loop has been passed from the forehead through each canthus into the lower lid, and when attached to the frontalis muscle a definite lift of the lower lid is obtained. All these methods undoubtedly give considerable improvement as regards the protection of the eye by the raising of the lower lid.

The use of the temporal muscle and its fascia promises to be a more satisfactory method of obtaining muscular movement for the paralysed eyelid. A flap of muscle is again cut, this time rather far forward, and a considerable amount of temporal fascia is taken with it. By splitting this fascia it may be made sufficiently long so that, while still attached to its original muscle, a strip can be passed to the upper and lower lids to meet at the inner canthus; at this insertion it may be fixed to the periosteum. When the temporal muscle contracts, this little flap squeezes the two eyelids together. The muscle action is, as a rule, not very strong, but quite sufficient to give a definite support to the lower eyelid.

The operative risks.—Too much care cannot be taken in cleansing the patient's buccal, orbital and nasal cavities from any potential septic foci, previous to operation. In addition, if the paralysis has been caused by mastoid disease everything should be done to make the mastoid cavity as aseptic as possible.

As regards the immediate pre-operative treatment, the surface of the skin and, in addition, the inside of the lips, and the tongue, and the roots of the teeth should be thoroughly cleansed with surgical spirit. At the commencement of the operation a sterile pack should be inserted between the lips and the teeth. In spite of all these precautions, in the writer's series, some mild sepsis has occurred in a proportion of cases, but usually in only one band among the various ones that have been implanted, e.g. the lowest band to the lower lip, or more frequently the upper band with its fixation to the front surface of the zygoma or in the malar region. In the latter case the cause is probably a mildly infected conjunctiva. To obviate this some antiseptic medicament should be applied frequently to the eye. Occasionally the band is passed too near to the mucous membrane of the mouth. In one case this was done by the writer, and the band eventually became exposed in the lower lip, owing to mucous membrane sloughing over the band.

Apart from sepsis affecting the band, hæmatomata are not entirely unpreventable in such an operation, and these may become infected. Trouble has also occurred in the form of serous exudate, which has eventually cleared up on the removal of a silk knot. Such infections have not, in the writer's experience, ever been acute, and have usually occurred after the seventh or eighth day, or even during the third week. Partial cosmetic failure of the operation may be due to the hold at the distal end of the band pulling on an atonic muscle. This frequently happens at the corner of the mouth, and less frequently at the point of fixation. The appearance in the writer's series of cases is often partially vitiated by a groove caused by one or other of the bands, particularly that to the lower lip.

The limit of cosmetic result.—Objective results: In a review of the cosmetic effect in the series under notice a very marked improvement is observed in all the cases, but in view of the lack of emotional response, the deformity, though mitigated, is by no means cured. The photographs are extremely difficult to standardize, other than those taken with the patient's face at rest, which in almost every case are satisfactory. It is obvious that it is almost impossible to obtain the same amount of facial expression at two different sittings to a photographer, and "before-and-after" photographs in this particular condition must be at present regarded as unreliable.

A Series of Twelve Cases Improved by Fascia Lata Sling Operations.

	Cause	Duration	Degree	Signs and Symptoms	Operation	Result and Present Condition
1	Removal of cervical tumour	8 years	Incomplete	Epiphora in cold weather. Drooping of right cheek. Drooping of angle of mouth. Overaction of left side.	Right internal canthoplasty. Insertion of facial slings into:— (1) Upper and lower lips (2) Temporal region. Purely supportive.	Subjectively: excellent. Objectively: good.
2	Operation for mastoid disease	8 ,,	Complete	Drooping of mouth. Eye removed for separate condition. Inability to close eye.	Fascial slings to upper eyelid, upper and lower lips and from temporal region to corner of mouth. Purely supportive.	Very good. Partial recovery of muscle movement.
3	Removal of tumour involving facial nerve	4 ,,	Complete	Inability to close eye. Epiphora. Sagging of mouth and sagging of cheek. Dribbling.	Fascial slings to upper and lower lips, angle of mouth and temporal region. Purely supportive.	Objectively: improved. Subjectively: Excellent result.
4	Anterior poliomyelitis	25 ,,	Complete	Inability to close eye. Sagging of right cheek.	(1) Triple fascial slings to upper and lower lips, and angle of mouth. Purely supportive. (2) Temporal muscle turned down and attached to slings, giving combined support and movement.	After (1) marked improvement subjectively and objectively. After (2) good movement of right side of face. Great improvement.
5	Operation for mastoid disease	23 ,,	Complete	Epiphora. Inability to close eye. Marked sagging of cheek and angle of mouth.	(1) Triple fascial slings. Purely supportive. (2) Temporal muscle added to slings and these shortened. One year after (1). (3) Shortening of muscle-belly and bands. Muscle fascial grafts to eyelids.	After (1) much improvement but still some sagging of mouth. After (2) and (3) subjectively and objectively improved.

6	? Mastoid abscess	40 ,,	Complete	Epiphora in cold weather. Inability to close eye. Sagging of cheek and angle of mouth. Biting of cheek.	Four fascial slings inserted from temporal region to right ala, upper lip, angle of mouth, lower lip. Purely supportive.	Excellent result.
7	Bell's palsy	19 ,,	Incomplete	Epiphora in cold weather, Sagging of mouth and cheek.	Triple slings to upper and lower lip, and from temporal region to angle of mouth. Sling to upper eye-lid. Purely supportive.	Subjectively: Good. Objectively: Fair.
8	Cholesteatoma petrous temple	2½ ,,	Complete	Epiphora in cold weather. Inability to close eye. Sagging of left cheek. Sagging of angle of mouth.	Triple slings to upper and lower lip, angle of mouth, and temporal muscle transplant to separate sling. Combined supportive and muscular.	Subjectively: Affords great comfort. Objectively: Good movement.
9	Bell's palsy	26 ,,	Complete	Epiphora in cold weather. Inability to close eye. Sagging of mouth. Biting of cheek.	Double fascial slings to upper and lower lips and angle of mouth from temporal region. Partially supportive.	Subjectively: Marked improvement and affords great comfort. Objectively: Good.
10	Operation for mastoid disease	11 ,,	Incomplete	(Had bad fascial hypoglossal anastomosis with good results.) Inability to close eye. Dribbling. Sagging of corner of mouth.	Triple slings to upper and lower lips, angle of mouth to temporal region.	Subjectively: Definitely improved.
11	Operation for mastoid disease	3 ,,	Complete	Inability to close eye. Slight sagging of mouth. Biting of cheek. Overaction of sound side.	Triple slings to upper and lower lips and temporal region with temporal muscle transplant into separate sling. Supportive and muscular.	Subjectively and objectively good.
12	Operation for mastoid disease	6 mths.	Complete	Epiphora in cold weather. Inability to close eye. Sagging of corner of mouth.	Triple slings to upper and lower lips and temporal region with muscle transplant into separate sling. Supportive and muscular.	Subjectively and objectively excellent. Good movements.

The best cosmetic results in the writer's series have been obtained with the temporal muscle-flap operation.

Subjective results: The patients themselves invariably volunteer the statement that their faces feel much more comfortable with the support that has been provided to prevent the overaction of the sound side. The psychological effect is also one of considerable value even when, to the surgeon, the cosmetic effect is disappointing.

The choice of case.—The writer believes that in all cases of facial paralysis some form of fascial support is indicated. It is to be hoped that nerve-grafting will progress by leaps and bounds; but even in these cases the fascial support would seem to be the most rational means of splinting the paralysed muscle during the period of recovery.

One may say that the scars produced in inserting the bands are negligible.

In the group of cases in which nerve-grafting gives no hope—i.e. when there is no response to faradism—the temporal muscle activation is an operation which should be definitely considered. Various writers have described operations for using strips of the masseter to activate the facial group, and this muscle certainly appears to the writer to have some advantages over the temporal muscle to the lower group.

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Mr. Lionel Colledge said that there was one point on which perhaps Sir Charles Ballance might like to say something more, and it arose out of the investigation of these cases. Sir Charles had shown that after a certain period the nucleus of the facial nerve degenerated. The operation of nerve-grafting had, in the cases shown, been performed fairly early—soon after the injury or accident which caused the paralysis, and presumably, judging by the excellent results, the nucleus had either not degenerated, or had only done so to such an extent that recovery was still possible. But he (the speaker) thought that after degeneration had been present for some time, however successful the nerve-grafting might be in itself, the nucleus would be permanently damaged, and such a result as those shown would not be possible. Would Sir Charles say after what period he thought the operation could succeed, because if that operation was not practicable, he (the speaker) supposed it would still be possible to carry out anastomosis with another nerve—one in which the nucleus was still intact. Or, alternatively, certainly after many years, the operation Sir Harold Gillies had demonstrated would still be possible.

He did not know whether Sir Charles Ballance thought that the old anastomosis was entirely a thing of the past, or that it still had its uses. One now saw fewer of these cases, but most of those sent for advice or operation were in his (Mr. Colledge's) experience, old ones, and in which a fascia lata graft would be more applicable.

Mr. E. Watson-Williams said that he had performed the operation of facial-glossopharyngeal nerve-grafting on three occasions, and in 1927 he had shown two of the patients at a meeting of the Section in order to demonstrate the degree of voluntary movement obtained.[1] Turning to the question of decompression of the facial nerve within the canal, the difficulty was that one so rarely saw a case in which the need for this procedure was at once apparent. Only twice had he had such cases, and in both the post-operative result had been perfect; he had shown one of the patients before at a meeting of the Section in 1929.[2]

Did Sir Charles Ballance advocate early decompression of the nerve in every case of facial paralysis due to cold or to herpes? A large proportion of these cases recovered spontaneously.

If one was contemplating intracanicular nerve-grafting, how long should one wait before deciding to operate? By an extraordinary coincidence he had had within one month three children brought up with mastoiditis and facial palsy; all were treated by simple (Schwartze) mastoidectomy. In none of the cases did the operation afford any explanation as to why the paralysis had occurred. One patient had begun to recover three days after the operation, and had completely recovered in three weeks' time; another, after three weeks, had just begun to recover, and was making steady progress; the third, paralysed eleven days before the operation, had shown no change in a month. Was the method of "preparing" a nerve for use as a graft to divide it and leave it to degenerate? And if so, how long before using it should this be done?

Mr. Sydney Scott said that it was necessary to discriminate carefully in the choice of the procedure to adopt for facial palsy, and to ascertain the site of the lesion before deciding what method to employ. A central ganglionic lesion of the facial nerve would not be improved by a nerve-graft.

A traumatic lesion of the facial nerve below the geniculate ganglion should be a type of case suitable for a nerve-graft, provided both ends were identified. When, as Sir Charles Ballance and Dr. Duel advocated, the external cutaneous nerve of the thigh had been divided and isolated a fortnight before transplantation, he (the speaker) had found it advisable to slip a small rubber tube over the distal end of the divided nerve, and close the incision. This enabled one to find it much more easily a fortnight later, when cutting down to remove a section for the graft.

Sir Harold Gillies' procedures were valuable, whether a nerve-graft were ultimately employed or not.

Mr. Thacker Neville said that when he had been working in China before the Great War he had anastomosed the spinal accessory nerve with the facial nerve in several cases. His most prominent success was in a missionary who was afterwards able to preach with his face straight if he raised a book in his hand.

Later, when he had joined the Army, Sir Charles Ballance was his consultant, and when in Malta he had seen Sir Charles performing an anastomosis; this had been a further stimulus to him (the speaker) in his work. When making an anastomosis he used to bury the anastomosed ends in the posterior belly of the digastric muscle. The anastomosis with the spinal accessory was a successful operation, so he had never aspired to complicated operations, as, e.g. that with the descendens noni.

Then came the fascia lata operation, which appealed to him, and he had carried out four. In only one case had sepsis occurred, and that was through his own fault in operating on a patient with a discharging ear. The three others had been successful (see reports on p. 109). They showed the result of using the fascia lata as an internal sling to enable the muscles to recover.

1 *Proceedings*, 1927, xx, 1439 (Sect. Otol., 59).
2 *Ib.*, 1929, xxii, 1410 (Sect. Otol., 98)

The technique of the operations was an exaggerated aseptic technique, similar to that followed by Sir Arbuthnot Lane when bone-plating, i.e. no part of an instrument which had touched the gloved hand must be allowed to go into the wound, and in these operations he (the speaker) sterilized the instruments at least five times, re-sterilizing before the insertion of each graft, and the towels were repeatedly changed. The dangerous site with regard to sepsis was the corner of the mouth.

He used intratracheal anæsthesia, inserting the tube himself. He did not go round the mouth with one graft as Sir Harold Gillies did; he used five grafts, and that was why he re-sterilized the instrument five times; he took two hours for the operation. He thought the secret of success was to employ this exaggerated aseptic technique.

He had not tried the facial nerve-grafts which Sir Charles Ballance had shown. He understood that Sir Charles used gold foil for covering the grafts, and he asked whether the foil was left in to be covered by granulations or whether it was removed after a time. Was it dental foil?

Dr. Douglas Guthrie said that only once had he carried out the operation which Sir Harold Gillies had described, but from that single operation he had learned much.

The patient was a young woman suffering from facial paralysis following a mastoid operation, and there was much scarring below and in front of the ear, so that operative exposure of the peripheral end of the facial nerve was impossible. The main deformity was drooping of the angle of the mouth. The operation consisted in introducing a fascial sling to support the angle of the mouth, in the manner described by Sir Harold Gillies. The graft passed across to the healthy side—an essential point—and a flap of temporal muscle was cut. The result was satisfactory, and the patient had since done fairly well, her appearance being much improved.

Dr. Guthrie asked whether Sir Harold had any difficulty in securing the mobility of the graft or grafts which he used, as it occurred to him (the speaker) that a flap of muscle turned down in this way would become fixed by dense fibrous adhesions. In his own case there was little mobility, though the angle of the mouth was supported. Did Sir Harold wrap this muscle upon itself, so as to have a fascial covering to the raw muscle surface, or did he take any other measures to ensure mobility?

He believed that Sir Harold passed his graft just below the mucous membrane, deep to the skin and to the muscles of the face. He (the speaker) had passed the strip of fascia only below the skin; this, he now thought, was a mistake, as, though the result was good, a visible ridge of fibrous tissue remained.

He further asked how Sir Harold ligatured one graft to the other, i.e. the graft crossing the face to the graft passing around the mouth. Fascia was a very slippery tissue; if one simply sutured one end to the other the suture material was liable to slip off.

Mr. Holt Diggle said he would like to know whether Sir Harold Gillies had given up associating this type of sling operation with face-lifting, i.e. whether he found that after putting in a tight sling there was a redundancy of skin, which required lifting. Or had the lifting of the face been given up?

Sir Charles Ballance (in reply) said that before the War he had performed some of the operations which Sir Harold Gillies had described, e.g. such operations as lifting a portion of the temporal muscle, or a portion of the anterior edge of the masseter, as described in 1911 in a paper by Professor Eden of Jena which had come to his notice some years before the Great War. Professor Eden

mobilized the anterior part of the masseter, carefully avoiding injury to the masseteric nerve; he (Sir Charles) passed it across the face and anchored it to the angle of the mouth. Eden also passed the slip from the temporal muscle to the lower eyelid. He did not think he had himself ever done that operation, but he had been struck, in these facial palsies, with the fact that the lower eyelid was depressed, and one of the things the skilled observer saw was white conjunctiva below the cornea.

The other method was that of Busch, which was published in 1910. In this a bronze wire was passed round the zygoma, and brought out at the upper lip. He (Sir Charles) had used that method, but he substituted very fine platinum wire, such as was employed in the laboratory. Platinum was not acted upon by the tissues, and he believed that his results had been made better by the use of the anterior portion of the masseter muscle, and the wire. He still thought that the wire method was an excellent one to attempt, though he would not say it was better than had been described by Sir Harold Gillies, but those who were *not* "Gillies" might try the Busch operation by using platinum wire.

The answer to Mr. Colledge's question about the nucleus could be given clearly. In long-standing paralysis it was known that the opposite Rolandic cortex atrophied. If the speech centre was destroyed in early life, the cells of the opposite cerebrum took up its function. Mr. Colledge wanted to know what happened when the medullary nucleus was completely destroyed. If one performed an operation for the relief of facial palsy when the nucleus was destroyed, he did not think it made any difference. He (Sir Charles) had carried out many operations for facial palsy two, three, five years after the onset of the palsy, and with success, and in those cases the medullary centre, and probably also the cells of the facial area of the opposite Rolandic cortex were gone, but the operations had been a success.

In none of his cases of facial palsy had the patient died; indeed, he thought that, except in cases of fractured base of the skull, he had never known an autopsy on a facial-palsy case. If any members came across a fatal case of facial palsy it would be of great importance to have it fully reported, especially in regard to the medullary nucleus.

Mr. Watson-Williams apparently agreed about decompression, but asked when it should be done. He (the speaker) supposed that in cases in which cold was the cause of the paralysis, and also in those in which the geniculate ganglion was inflamed, perhaps 85% to 90% of the patients recovered without anything being done. If at the end of three months it was found that there was no response to the faradic current, it would be ridiculous to wait longer—he, personally, would not wait so long, but three months was the limit. In the past, surgeons seemed to have waited months and years before suggesting treatment in cases of surgical facial palsy, whereas it was now known that wonderful results ensued if medical treatment was given up and an early operation performed. There could be no doubt that the earlier the operation was done, the nearer perfection was the result, and also that the younger the patient, the better was the result, and the more rapid was the recovery.

Mr. Watson-Williams had also asked about otitis and suppuration. If one was going to use a graft it did not matter if suppuration was present; but what was important was that the surgeon must himself do the dressing every day.

With regard to Mr. Thacker Neville's question about gold-leaf: that was put on at the time of the operation in order to prevent any drag on the graft region in the process of dressing. It was removed seven days afterwards. One could not then see the graft, but continued to dress the wound. If the surgeon did the dressing gently himself it would be a success; if he handed this over to a dresser who did not know anything about it, or to a nurse, no surprise need be felt if it failed.

As to the preparation of the graft, Cajal mentioned from eight to twelve days.

In his (Sir Charles's) own work from ten to twenty days was the time. Dr. Duel, when he had two cases in hand, would sometimes take a nerve from one patient to graft both. That was not a good plan unless a blood test was carried out beforehand to ensure that both belonged to the same blood class, but both Dr. Duel's patients had done well. In his paper he described the preparation of the graft. The degenerated graft was in such a condition as to be particularly favourable to the passage along the empty tubes of the degenerated graft of the axons of the central segment of the nerve.

Mr. Sydney Scott had asked what happened if the lesion involved the geniculate ganglion. He (Sir Charles) did not think that mattered. [Mr. Scott: If you have a case with a fractured base, must you do the old anastomosis?] Yes, that was so. He had had cases of gunshot fracture of the mastoid in which the whole region was destroyed, and one could not perform the new operation on the injured nerve in the aqueduct because the nerve had been blown away.

Sir Harold Gillies, in reply to Dr. Guthrie, said that the new muscle belly was completely surrounded with fascia as described in the paper. The method of suturing one graft to another was by transfixion with a needle threaded with chromic catgut for the primary knot, and subsequently the fascia was passed round the fascia, or through it, so as to make it quite secure. He had not found any difficulty on this score.

In reply to Mr. Holt Diggle: It was advisable to remove a wedge of skin in the pre-auricular temporal region when there was an excess of skin; but in his opinion that did not permanently aid the alleviation of the facial paralysis.

He (Sir Harold) was delighted with the remarks that had been made about his paper, and the kind reception which had been accorded to it.

Three Cases of Facial Paralysis treated by Temporal Muscle Graft and Fascia Lata Control.—Sir HAROLD GILLIES, C.B.E., F.R.C.S.

I.—G. M., male, aged 20.

History.—August 1930. Mastoid operation.

First seen, 16.6.33.—Complete right facial paralysis.

Operation, 27.10.33.—Figure-of-8 loop fixation of upper and lower lips. This loop was drawn upwards and backwards by two further strands of fascia, one being fixed deep to the zygoma, forming a rigid support, while the other was passed superficial to the zygoma and attached to a turned-down flap of temporal muscle.

Operation, 17.11.33.—Strip of temporal muscle and its fascia passed forwards to embrace the upper and lower eyelids.

Complications.—Slight slackness in the pulling-back effect. Muscle movements present but poor; possibly the stay suture was a mistake.

II.—F. B., female, aged 27.

History.—At age of 9 months, mastoid operation. Nerve not cut but it was seen and found to be definitely necrotic at operation. Left-sided facial paralysis developed during childhood. One year's electrical treatment.

First seen, 13.3.30.—Required fascia lata sling operation.

Operation, 9.4.30.—Three fascial loops passed from incision in upper parotid region to (1) angle of mouth, (2) centre of upper lip, (3) centre of chin.

Result: Improvement, especially when at rest, but there was failure of the middle band to hold the corner of the mouth. Referred to Dr. C. B. Heald for electrical treatment.

Operation, 3.3.31.—Fascia sling uniting corner of mouth to temporal muscle. Result: Improvement. Further electrical treatment.

Operation, 20.3.34.—(1) Muscle fascial graft to eyelids, (2) old bands and muscle belly hitched up, (3) excision of excess skin, (4) excision of excess mucous membrane from lower lip.

Complications.—Marked groove effect of the fascia pull, especially of the lower band. Muscle movements strong. Eyelid result good.

III.—J. T., male, aged 8.

History.—14.3.33, admitted to Downs Hospital with chronic mastoid disease, having had ear discharge for three years. Mastoid operation, April 1933. A small fistula was found passing through the posterior wall of the meatus into a diseased cell behind the bridge, very near to the plane of the facial nerve. During removal of the diseased bone the nerve was damaged, and facial paralysis was noticed as soon as the boy came round from the anæsthetic.

First seen, 20.10.33.—During the six months since operation no signs of recovery, in spite of treatment with massage and electricity.

No reaction to faradism at any time. Mastoid wound healed.

Operation, 16.2.34.—Strip of temporal muscle turned down on right side over zygoma. Fascial strip sutured to undersurface and passed through to corner of mouth and forward, at which point it was attached to a figure-of-8 loop, embracing the affected circumoral group.

Complication.—Slight serous exudate from corner of mouth, causing depression or groove. Effect, a good muscular movement.

Three Cases of Facial Paralysis.[1]—W. S. THACKER NEVILLE, F.R.C.S.Ed.

I.—W. S., aged 33, fireman on an engine, on August 7, 1931, was coupling-up a train and was caught behind the right ear by the vacuum pipe. Result: facial paralysis. The eye could not be closed and therefore the patient was unable to perform his work.

January 1, 1932: Fascia lata graft inserted into the lower eyelid and also into the upper eyelid. Result: eye aperture reduced to a small slit which patient was able to close. Consequently he was able to resume work in April 1932.

II.—C. L., aged 32, came to hospital September 1, 1931, complaining of tinnitus, vertigo, and deafness of the left ear. Said life was intolerable.

27.10.31: Radical mastoid operation performed.

3.11.31: Labyrinthectomy performed, with destruction of the cochlea. Paralysis of facial nerve.

11.11.31: Fascia lata graft to face.

24.11.31: Fascia lata graft operation repeated.

3.2.31: Fascia lata graft to upper and lower eyelids.

III.—A. J., aged 35, complained of otitis media, tinnitus, and vertigo.

17.8.32: Left radical mastoid operation—destruction of labyrinth—cochlea opened—(Hinsberg's operation). Paralysis of facial nerve.

31.8.32: Muscle graft to mastoid cavity.

7.12.32: Fascia grafts inserted from above left temporo-mandibular joint to corner of the mouth and from temporal region through upper and lower eyelid to inner canthus of left eye.

[1] Shown at the Meeting of the Section held on May 4, 1934.

Treatment of Facial Paralysis. A Case of Facial Nerve-graft by the Duel-Ballance Method.—C. HAMBLEN THOMAS, F.R.C.S.Ed.

E. B., male, aged 59. First seen June 1932 with left facial paralysis secondary to left chronic suppurative otitis media. Radical mastoid operation performed; no improvement with regard to the paralysis by October 1933 in spite of massage and electrical treatment. At this time there was galvanic response in the left face muscles but no faradic response.

November 2, 1933: Admitted to hospital. Preliminary exposure of facial nerve hiatus, and graft from leg isolated.

November 14: Graft transferred to hiatus in facial nerve.

December 9: Faradic response of levator anguli oris noticed. All facial muscles on left side show brisker response to galvanic stimulation.

January 25, 1934: Faradic response of levator labii superioris alæque nasi. Galvanic reaction improved.

April 23, 1934: All reactions stronger but no further spread of faradic response.

Section of Radiology

President—R. S. PATERSON, M.D.

[*February* 16, 1934]

DISCUSSION ON RADIODIAGNOSIS IN DISEASES OF CHILDREN

Dr. BERNARD SHIRES read a paper on **"Radiodiagnosis of Chest Diseases in Children."**

He showed a table illustrating the association of lung disease with asthma. With regard to tuberculosis, he said that it was not possible to establish a positive diagnosis of tuberculous infection by radiography alone.

Mediastinal shadows, again, were difficult to interpret, and the origin of a gland lesion in the mediastinum could not be established radiographically. Help might be afforded by radiotherapy, as certain mediastinal growths responded to X-ray treatment and thus revealed their nature.

The Radiological Appearances of Certain Bone Dyscrasias in Infancy and Childhood.

By C. G. TEALL, M.B.

In the short time at my disposal I shall restrict myself to the consideration—all too brief I am afraid—of certain bone dyscrasias which may be of interest to radiologists who do not have the opportunity to work in a children's hospital, for although I have seen most of these conditions with reasonable frequency at the Children's Hospital, Birmingham, I have seen them only rarely at the general hospital to which I am attached.

The first condition to which I would draw your attention is rickets. Rickets is a deficiency disease characterized by an imbalance of the calcium/phosphorus equilibrium of the blood, due to a deficiency of vitamin D. It is a general disease of metabolism and affects the whole body, but its effects are seen to a remarkable degree in the bones, which not only serve as an indication of the type and severity of the disease, but also supply reliable information as to its progress and cure. Not only do the bones show signs of the development of rickets at a very early stage in the disease, but at an equally early stage they show evidence of a commencing healing.

For the purpose of establishing the presence of rickets, the anterior ends of the ribs would, owing to their structure, supply the earliest radiographic evidence, but unfortunately their situation does not allow of a sufficiently accurate examination. In actual practice, therefore, one chooses to examine the lower ends of the forearm bones, for the reason that they are superficially placed and not obscured by overlying tissues and can be examined with reasonable ease even in a fretful, ill child. Just how tiresome a child with rickets can be, from the radiologist's point of view, only those who have to examine such children know. Considerable patience is required, for good films are essential in order to make a diagnosis in an early case, and one of the signs of rickets—cupping of the bone-end—can easily be simulated by incorrect

positioning. I would mention at this point that in my experience, patience and tactful handling of the patient are far more useful than any form of restraining apparatus, in radiography of children.

The earliest signs of rickets are seen at the ends of the long bones, but it is necessary to look at the quickly growing end and not at the slowly growing one. While in experimental rickets the earliest sign is a widening of the epiphyseal line—a very useful sign in the examination of rats for instance—this is not sufficiently evident in young children to be of diagnostic value, for the reason that only a small proportion of the epiphysis is ossified. The earliest sign is that the end of the metaphysis, which normally is quite smooth and regular, becomes frayed. If the child is very ill and lies still, whilst the fraying will become more pronounced and the epiphyseal line become obviously wider than normal, the appearance of the bone will not pass on to the pronounced stage of obvious rickets seen in more active children and indicated by the characteristic cupping of the end of the metaphysis. The end of the shaft becomes splayed out and curved round the epiphysis and has the appearance of a champagne glass. This cupping is more pronounced in some bones than others, and depends on their normal shape ; it is well seen in the lower end of the radius—and even better in the lower end of the ulna—but it is not seen where the end of the bone is normally convex—the lower end of the humerus for instance.

While in the early stage of the disease one has to look at the end of the bone for radiographic evidence, as the condition progresses changes in the shaft of the bone make their appearance. There is a general diminution in the density of the bone which in advanced cases may be very marked, so that the bones may look, as Park has so admirably described them, like ghosts of themselves. The bone trabeculæ become opened out and coarse, and gradually the cortex becomes indistinguishable. At the same time the periosteum is laying down osteoid, although until healing commences this is not visible, owing to lack of calcium. The shaft of the bone is very fragile, and multiple fractures occur which may be discovered for the first time at the radiographic examination.

In the skull one finds evidence of craniotabes, although in my experience this has not been so obvious radiographically as it appears to be clinically. It is usually seen on the posterior aspect of the skull.

With appropriate treatment rickets can be cured, and evidence of healing is very soon seen in a change in the radiographic appearance. A linear shadow appears behind the epiphysis, distal to the point where the metaphyseal bone ends. It is due to the provisional zone of calcification and, of course, appears at the point which corresponds with the end of the metaphysis, the explanation of the gap between it and the apparent end of the shaft of the bone being that this is occupied by osteoid laid down during the course of the disease which does not contain calcium and therefore does not show on a radiograph. As healing progresses this gap is gradually filled in as calcium is laid down, and eventually it becomes filled with a dense mass of trabeculæ. The bone which is laid down from the time when healing commences is, as one would expect, normal, but the bone which replaces the osteoid in this gap is recognizable for from twelve months to two years afterwards, and forms a useful clue in healed cases, when other evidence is lacking that the child has had rickets. When healing commences at the end of the bones calcium is also deposited in the subperiosteal osteoid, and periosteal layering becomes evident.

With adequate treatment an average case of rickets will be cured in about twelve weeks, and even in severe cases healing may be quite rapid. I know nothing more remarkable in radiography than the rapid change in a case of severe rickets—from the stage of intense decalcification and multiple fractures to complete healing—in such a comparatively short time.

While simple rickets occurs in infancy and heals in this way, there are other

varieties of simple rickets which either appear later in childhood—true late rickets, a condition which would appear to be of extreme rarity—or which appear in infancy and fail to heal—chronic or resistant infantile rickets.

Most of the cases of so-called late rickets are due to one of two conditions. (1) Chronic renal disease—usually chronic interstitial nephritis—in which rickets is associated with renal infantilism. (2) Cœliac disease—in which the infantilism is at certain stages associated with the presence of rickets, while at other stages rickets is absent.

I am rather of the opinion that there is another type, but at present I am not in a position to make any further observation than the fact that certain cases do not appear to fall under the heading of either renal rickets or cœliac disease.

(1) *Renal Rickets.*—I have described the bone changes in renal infantilism at some length in a previous communication to a Section of this Society.[1] Although it is a true low-calcium rickets, the appearances may be quite different from those seen in simple rickets. There appear to be two clearly defined types of rickets to be seen in renal infantilism: (*a*) One in which the bones have an appearance like that seen in simple rickets and may show improvement at such times as the renal function improves; (*b*) one in which there is a perfectly typical radiographic appearance which is diagnostic of renal rickets. This has been described by Professor Parsons and myself as the "woolly type." The changes are best seen, as in ordinary rickets, at the rapidly growing end of the long bones, but are not in the least like those seen in simple rickets. In the metaphysis one sees evidence of irregular ossification with a stippled, woolly appearance. The end is not splayed out but, owing to the laying down of irregular subperiosteal masses of osteoid, the bone shows an eaten-away appearance under the periosteum. The shaft of the bone shows osteoporosis with coarse trabeculæ, but remains straight—the extraordinary deformities seen in this disease arising from collapse in the metaphysis, owing to the absence of supporting bone. The changes in the bone are not seen to an equal extent throughout the long bones, nor are they symmetrical. In addition to the changes in the long bones there are changes to be seen in the skull bones, which vary from a woolly stippling to an extraordinary degree of bone change not unlike that seen in an advanced stage of Paget's disease.

(2) In *cœliac disease* the bones show a general osteoporosis with widely separated and very irregularly arranged trabeculæ towards the ends of the long bones. In the same areas there are often a number of dense transverse lines. While the appearance is not absolutely diagnostic of cœliac disease, one comes to recognize a type of bone structure which one associates with this disease. When the child commences to grow as a result of treatment rickets develops which conforms to the simple type of rickets superimposed on the already altered bone structure, but whereas in renal rickets the exhibition of antirachitic remedies has no effect—or may actually make the condition worse—in cœliac rickets it will bring about healing.

Another deficiency disease which concerns the radiologist is *scurvy*, for here again the bone changes are diagnostic. The bones show a thin cortex and a general atrophy in which the trabeculæ disappear, and they assume what has been described as a ground-glass appearance. Characteristic changes occur at the bone-ends. All the bones are affected, but the changes are particularly well seen at the lower end of the femur. The zone of provisional calcification is sharply defined and much more dense than normal. This, the Trummerfeld zone, is all the more obvious, for the reason that immediately behind the dense area there is a zone of lessened density—the Gerüstmark zone—in which all the bone structure disappears. The so-called epiphyseal separations which occur in scurvy are actually fractures in the metaphysis which occur through this decalcified zone, the dense Trummerfeld zone

[1] *Proceedings*, 1928, xxi, 717 (Sect. Electrotherap., 25).

being separated together with the epiphysis. When separation occurs the dense calcified area may be moved laterally in relation to the shaft and this, together with calcification spreading out under the periosteum—which is detached if hæmorrhage has occurred—will give rise to the bony spurs which are characteristic of scurvy. In the early stages the subperiosteal hæmorrhages show no evidence of their presence on a radiograph, and it is not until calcification occurs beneath the separated periosteum at a distance from the shaft that they can be detected. The hæmorrhage commences at the end of the shaft and gradually strips up the periosteum towards the middle of the bone—and when hæmorrhages occur at both ends the periosteum may in this way be lifted from the whole length of the shaft of the bone.

In addition to the dense limiting line to the metaphysis, the epiphysis also shows a similar dense line at its periphery, as do also the small bones of the carpus and tarsus. Here again the appearance of this dense line is accentuated by the structureless bone which it surrounds. These dense lines in the epiphyses and small bones will persist for a very long time—years in many cases—and provide evidence that a child has had scurvy, long after other traces have disappeared.

Congenital syphilis.—I do not propose in this paper to deal with the inflammatory diseases of bone, but in view of its importance in differential diagnosis I shall deal with the appearance seen in the bones in congenital syphilis. Three types of lesion are found in this condition, osteochondritis, osteomyelitis, and periostitis. Of these the changes due to osteochondritis are the most important. They are seen in the metaphysis, which shows a dense shadow at its extremity, with rarefaction in the bone behind this, varying greatly in its extent—there may be only small localized areas or it may extend completely across the bone. Later on, irregular dense fraying is seen at the metaphysis—the saw-tooth appearance, which according to McLean, is pathognomonic of syphilis in the absence of all other signs. As in the case of scurvy, the so-called epiphyseal separations are really fractures through the much weakened metaphysis. Osteomyelitis occurs as localized areas in the diaphysis, which may appear as punched-out areas on the edge of the bone, as seen in the radiograph, or they may be associated with localized periostitis. Periostitis may occur either independently of the other lesions or in association with both of them. Areas of local thinning of the bones of the skull occur in congenital syphilis, but whether these occur in the absence of associated rickets is debated.

From what has been said it is clear that while in typical cases the diagnosis may be quite evident, in certain cases difficulty may arise in distinguishing, on the radiographic examination alone, between rickets, scurvy and congenital syphilis. Bony spurs and periosteal layering occur in all three conditions, and metaphyseal fractures occur in both scurvy and congenital syphilis. In general, however, it may be said that in congenital syphilis not only are the bone changes much more irregular than in rickets and scurvy, but they are much more irregularly distributed throughout the bones of the body.

I now pass to the consideration of certain disturbances of the growth of the bones in children.

(1) *Achondroplasia.*—This is a disturbance of bone growth in which bone formation in cartilage is arrested—it is an aplasia as opposed to a dysplasia—but periosteal bone formation is normal. This causes marked shortening of the limbs, while the trunk may be approximately normal in length. The cause is unknown, and although in the past it has been called fœtal rickets, it has no connexion with this disease.

Radiographs of the long bones show an apparent thickening of their shafts, but actually the thickness is normal for the age of the child, and it is their abnormal shortness which gives this impression. The metaphysis is cupped in the case of young children, who have large cartilaginous epiphyses, and later, as the epiphysis becomes ossified, the epiphyseal line is seen to be much narrower than normal.

PLATE I.

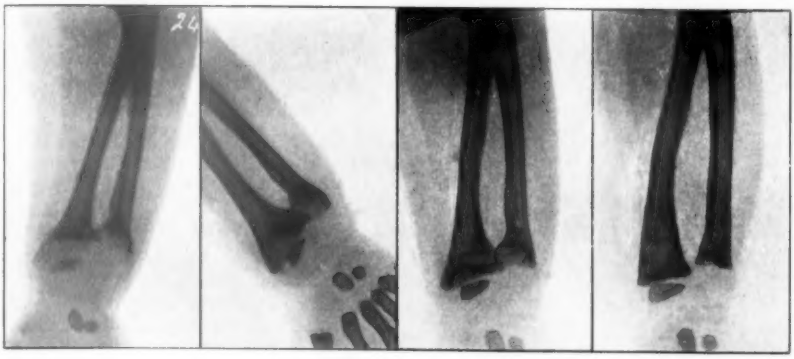

FIG. 1.—Rickets: showing active and healing stages.

FIG. 2.—Renal infantilism. Note the asymmetrical type of bone change.

FIG. 3.—Renal infantilism: showing changes in skull bones.

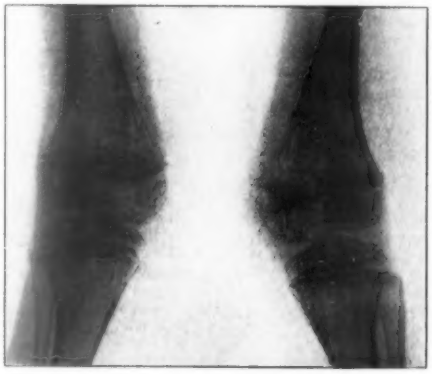

FIG. 4.—Cœliac disease: showing abnormal openwork bone trabeculæ.

PLATE II.

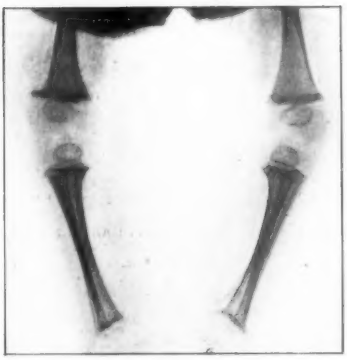

FIG. 6.—Scurvy with fracture in metaphysis through zone of rarefication, and subperiosteal calcification.

FIG. 5.—Scurvy.

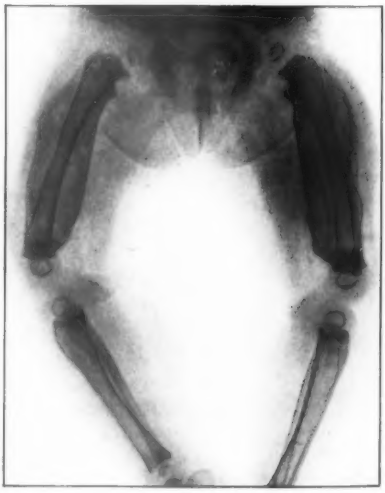

FIG. 7.—Scurvy. Showing calcium deposits in subperiosteal hæmorrhages.

PLATE III.

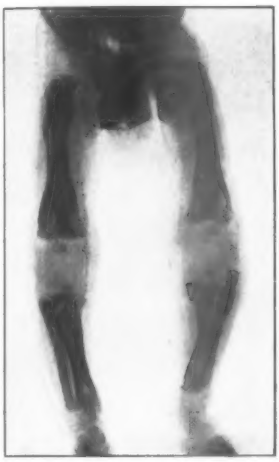

FIG. 8.—Congenital syphilis.

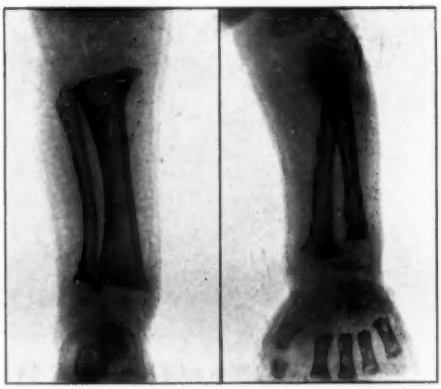

FIG. 9.—Achondroplasia. Note the cupping of the end of the metaphysis for the large cartilaginous epiphysis.

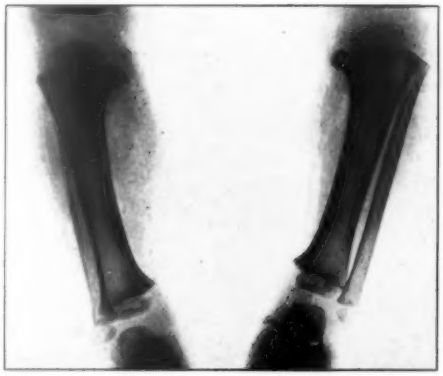

FIG. 10.—Achondroplasia. Showing the abnormally narrow epiphyseal line.

PLATE IV.

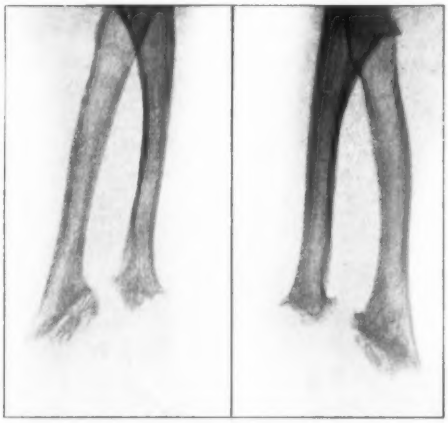

FIG. 11.—Dyschondroplasia. Note the unequal length of the paired bones and the obliquity of the epiphyses.

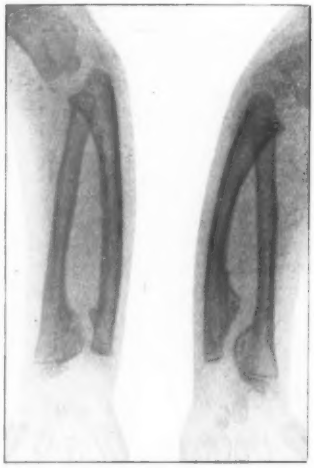

FIG. 12.—Dyschondroplasia. "Hereditary deforming chondrodystrophy."

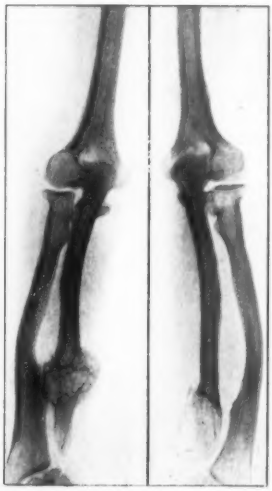

FIG. 13.—Dyschondroplasia. "Hereditary deforming chondrodystrophy." Mother of patient whose radiographs are shown in fig. 12.

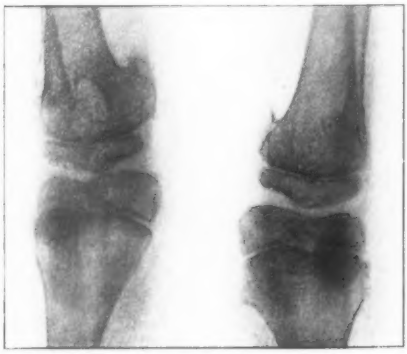

FIG. 14.—Dyschondroplasia. Multiple exostoses.

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FIGS. 15 and 15A.—Dyschondroplasia. Morquio's type.

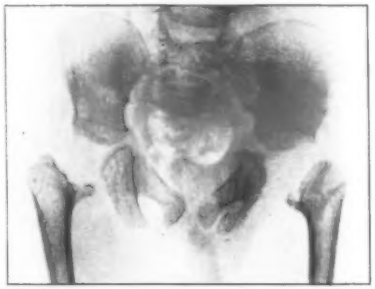

FIG. 15.

FIG. 17.—Osteogenesis imperfecta. Fœtal type. Note wormian bones in skull.

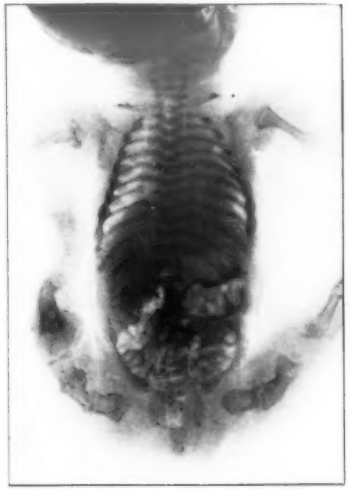

FIG. 16.—Osteogenesis imperfecta. Fœtal type.

PLATE VI.

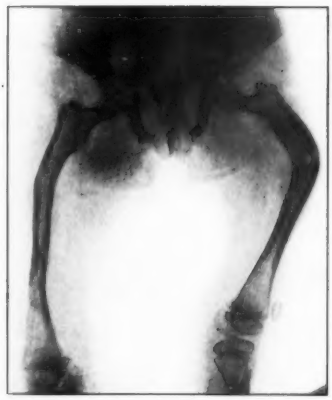

FIG. 18.—Osteogenesis imperfecta. Infantile type.

FIG. 19.—Osteosclerosis fragilis.

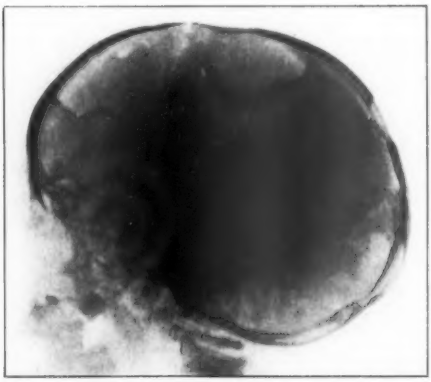

FIG. 20.—Xanthomatosis. Schüller-Christian's disease.

The bones of the vertebral column show similar changes, but they are much less marked. In the skull a premature synostosis occurs at the base, but the cranial bones are normal.

(2) *Chondrodysplasia*, on the other hand, gives rise to a far more varied picture. Various types of chondrodysplasia have been described by different observers and they are indicated by a variety of different names. Ollier's disease, hereditary deforming chondrodystrophy, multiple cartilaginous exostoses, diaphyseal aclasia and Morquio's dystrophy—the latter called after Morquio, although had particulars of the case which Brailsford showed at a meeting of the Electro-Therapeutic Section of this Society in 1928 been published a little earlier, it might have been associated with the name of one of the members of this Section. It now appears that even the osteopathia condensans disseminata described by Albers Schönberg also comes into the same category. However, since they are all due to a disturbance of bone growth which is congenital in origin and the cause of which is quite unknown, in the present state of our knowledge it seems best to group them all under one head, for all these different conditions are, so far as we know, only varieties of the same defect in bone growth, although its manifestations vary from multiple exostoses to changes in the internal structure of the bone.

Radiographs of the bones show, in varying combination, exostoses, irregular growth of the bone-ends, curvatures, and obliquity of the epiphyses which, although not primarily involved, may be affected secondarily and assume abnormal shapes. Paired bones may be of unequal length. The disturbances of growth are frequently asymmetrical and they may be almost entirely unilateral (as in the cases first described by Ollier). These changes can be appreciated much more readily by the study of the radiographs than by any description it is possible to give, as their variety seems to be legion.

(3) *Osteogenesis imperfecta*.—Disturbance of the periosteal bone formation gives rise to a different group of cases which may be considered under the title of osteogenesis imperfecta, although here again a number of different names have been used to describe conditions which are, so far as we know at present, essentially variations of the same pathological process, the cause of which is unknown. Osteopsathyrosis, fœtal rickets, annular rickets, fragilitas ossium, and periosteal dystrophy are all names which, together with osteogenesis imperfecta, have been applied to these cases which show an essential fragility of the bones as their outstanding characteristic.

Two types of the disease are recognized, the fœtal type and the infantile type, which show quite different radiographic appearances.

In the fœtal type the shafts of the bones are short and thick, and in many cases they show marked deformity—the result of old healed fractures which have occurred during intra-uterine life. In addition to the changes in the long bones, there are also changes to be seen in the skull, due to defective ossification of the cranial bones, which in typical cases show an appearance like a jig-saw puzzle, owing to the fact that they are largely made up of wormian bones. In the majority of cases of the fœtal type the infants are either stillborn or only live for a short time.

In the infantile type the child appears to be normal at birth, but later an extraordinary fragility of the bones manifests itself. This is usually noticed when the child commences to walk, when fractures occur as a result of trivial injuries; but in certain cases it may be delayed even to adolescence. In spite of the defective ossification of the bones these fractures unite fairly readily.

The radiographic appearance of the bones in cases of this type shows a marked contrast to that seen in the fœtal type. Instead of being thick, the bones are thin. They show a marked attenuation of the cortex, and considerable reduction of the normal trabeculation; they look fragile. In cases of some standing, deformities of multiple healed fractures are seen. There, is, however, no interference with the epiphyseal growth of bone and the thinness of the shafts of the bones is accentuated

by the fact that they attain their normal length, exactly the opposite to what is seen in achondroplasia.

(4) *Osteosclerosis fragilis.*—Another condition which is associated with an essential fragility of the bones is osteosclerosis fragilis. This, again, is a condition described in the literature under different names. Albers-Schönberg's disease, marble bones—rather a misnomer in view of their fragility—and osteopetrosis are all names applied to a condition which was originally described by Albers Schönberg in 1904. It is a rare condition—I have seen only one case at the Children's Hospital in fourteen years—and appears to be due to a primary osteosclerosis with secondary changes due to this—anæmia, splenomegaly, and optic atrophy.

The radiographic appearance of the bones in this condition is very striking. The affected parts of the bones show no ordinary bone structure, but a dense sclerosis which is quite opaque to X-rays, and gave rise to the name "marble bones," which has been applied to the condition. The areas of sclerosis tend to be towards the ends of the long bones, which sometimes show a uniform clublike appearance, but sometimes they occur as transverse bands across the shaft. The bone, which, as seen in the radiograph, looks abnormally strong, is in fact extremely fragile and breaks easily. All the bones in the body are affected, and the changes are well seen in the skull, where the sclerosis and thickening at the base accounts for the optic atrophy.

(5) *Xanthomatosis.*—In conclusion I should like to mention another rare condition in which the bones are affected secondarily, but which also produces extraordinary appearances—though of quite a different type—in the skull. The Schüller-Christian syndrome is one of the manifestations of xanthomatosis and falls in the same category as Gaucher's disease and Niemann-Pick disease.

The first cases of this condition were described by Schüller in 1915 and the next by Christian in 1919, who described what is now known as Christian's syndrome of "defects in the membranous bones, exophthalmos and diabetes insipidus." It was Rowland in 1928 who first established the fact that the condition was a disturbance of lipoid metabolism in which a deposition of lipoid (in this disease chiefly cholesterol) occurs in xanthoma cells throughout the reticulo-endothelial system. Collection of these xanthoma cells produce gummatous nodules. These occur in connexion with the dura and the periosteum, and also in the bone itself. These masses of xanthoma cells appear to have an extraordinary destructive effect on the bone, for wherever they grow, bone resorption occurs. The condition is not primarily a bone disease at all, but the bone is affected by a sort of pressure atrophy.

The chief bone changes are seen in the skull, although other bones may be affected in a lesser degree. There are extensive bone defects in the calvarium and also at the base of the skull, and the appearance is quite unlike that of any other bone disease with which I am acquainted. The appearance has been variously described as "map-like" and "moth-eaten" both of which terms are quite descriptive. The bone defects are clear-cut and the surrounding bone is normal.

I have mentioned this condition because although up to 1928 only twelve cases had been recorded, there are now records of about sixty. It seems possible, therefore, that as radiologists become more acquainted with the appearance that it produces, the condition may be found to be more common than was originally supposed.

One is constantly meeting with bone dyscrasias and alterations in bone structure which are mystifying and apparently do not fit into any of the known categories. In my experience it has only been by the co-operation of the radiologist and the clinician that we have been able to make advances in working out the bone dyscrasias in children. In the Children's Hospital at Birmingham I have been particularly fortunate in that my colleagues have taken such an interest in the radiological side of the work, and I should like to take this opportunity of recording my thanks to them all, and in particular to Professor Parsons, for the help that they have given me.

Dr. N. B. Capon said that the children's physician owed a great debt of gratitude to the radiologist, because of the difficulties of pædiatrics, the lack of symptomatology in many cases, and the occasional failure of the clinical examination to be a very thorough one. The physicians in Liverpool had the special advantage of working with the disciples of Thurstan Holland, whose skill and honesty had set an example which they followed very successfully. He, the speaker, agreed with Dr. Shires that the diagnosis of tuberculosis in its early stage was not possible in many cases by X-ray examination; it was of the greatest importance to take into account the history of the child's illness and the general appearance, to make a thorough examination, together with observations of the tuberculin reaction —particularly the intradermal reaction—and to search for organisms in the sputum or, if this was not obtainable, in the stomach washings. As to what the radiologist called evidence of an unresolved pneumonia—a small area of shadow—which often came as a great surprise to the clinician, he doubted very much whether these were pneumococcal areas. Very often in the history there was no clinical evidence of any attack of pneumonia, and when one followed the case up it happened that in from ten to fourteen days the shadow disappeared entirely. He believed that the shadow was due, not to the outpouring of exudate into the alveoli, but rather to small areas of collapse, and possibly in some cases to vascular changes such as congestion.

Dr. J. F. Brailsford said that the essential in radiography of children was speed. The less the child saw of the radiologist and his instrument and the sooner the radiologist made his instantaneous radiograph after the patient was brought into the room, the better and more uniform would be the radiography.

During the past ten years he (the speaker) had examined radiographically all the children submitted from the Infant Welfare Centres of the City of Birmingham; and though rickets was fairly common, scurvy was much less so and the bone dystrophies were relatively rare. The suggestion that these last should be termed dyschondroplasia was open to strong objection. Apart from being a big name which perhaps sounded somewhat impressive, it failed to indicate that the bone lesions previously included under this heading could be classified into very well-defined groups if one had had the good fortune to see examples of these groups at different age-periods as well as in infancy. There had been a tendency in the past to apply the term to every case which presented unusual radiographic features, and having done that, to take little further interest in the case. Though these groups presented definite characteristic clinical features the diagnosis was essentially based on radiographic appearances which he had already illustrated. Briefly the groups were:—

(1) Osteogenesis imperfecta; (2) Albers Schönberg's disease; (3) achondroplasia; (4) chondro-osteo-dystrophy; (5) multiple chondromata; (6) multiple exostoses; (7) dystrophies due to endocrine disturbances (thyroid, pituitary, pineal, parathyroid, adrenal, sexual glands; (8) dystrophies due to renal and cœliac disease.

Achondroplasiac patients were dwarfs having stunted but strongly developed limbs and characteristic skull and facial appearances, and the radiographs showed short thick tubular bones (including the phalanges) with well-developed tuberosities, but no irregularity in the appearance of the ossific nuclei of the epiphyses or their subsequent fusion with the diaphyses. The vertebral column usually showed little departure from the normal, but atypical cases occurred in which this was affected and others occurred in which all the bones of the forearm and leg only were shortened and broadened.

In the group which he had called chondro-osteo-dystrophy the patients were dwarfs having short necks, a prominent sternum, a dorsolumbar kyphosis and marked swelling of the limb joints. The radiographs of these patients showed, in childhood, increase in the joint spaces, multiple nuclei for the epiphyses and marked

irregularity of the ends of the diaphyses and of the vertebral bodies, particularly in the cervicodorsal and the dorsolumbar areas; and in adolescence marked deformity of the epiphyses—owing to the irregular ossification—resulting in their inability to withstand the normal weights, stresses, and strains. Eventually the multiple osseous nuclei fused, but the deformity caused during the plastic stage persisted. A number of these cases have been described in the literature as patients showing multiple foci of osteochondritis.

Patients affected with the condition of multiple chondromata exhibited a shortened limb. The dystrophy was regarded by Ollier as unilateral on this account but even his case, on radiographic examination, showed that, though clinically asymmetrical, the bone lesions were present on both sides. Clinically, therefore, the unilateral appearance of the dystrophy was quite distinct from the symmetry of the two former groups. Radiographs of these patients showed defects in ossification. The lesion in the bone failed to ossify and produced a cyst-like defect. Though the lesions developed in the diaphyses only—another distinctive feature from the two former groups—they sometimes interfered with the growth and development of the epiphyses, resulting in shortening of the markedly affected limb. Later in life isolated chondromata might result in spontaneous fracture or might undergo sarcomatous changes. Multiple exostoses became very apparent towards adolescence though radiographs in early infancy would reveal characteristic osseous tuberosities projecting from the sides of the diaphyseal extremities. Owing to the great development of some of these exostoses, marked deformity and limitation of the limb-joints might be seen, and in some cases the growth of the bones was interfered with and stunting of the limb occurred. Radiographically the lesions were found to be widespread throughout the skeleton. As in the multiple chondromata, the tumours developed in the diaphyses only, though they might interfere with the development of the adjacent epiphyses. The statement, copied from one textbook to another, that these exostoses developed from the epiphyses was incorrect.

All these groups of dystrophies showed a familial tendency. They were frequently found in several members of the same family and often showed a remarkable resemblance in the type, character and distribution of the lesions.

He (Dr. Brailsford) emphasized the importance of appreciating the marked irregularities in ossification of the young skeleton, due to thyroid insufficiency, as a number of such cases had been described as examples of osteochondritis. A study of the skeletons of cretins would convince anyone of the significance of this factor.

The possibility of a slipped femoral epiphysis being due to renal rickets he had pointed out previously.

Dr. Teall had described the condition which—if it must bear any man's name—should be called Schüller's disease after Professor Schüller of Vienna, who first drew attention to the remarkable map-like radiographic appearance of the skull, which was typical and diagnostic of xanthomatosis. Every radiologist should make himself familiar with it. Four years later than Schüller, Christian described the syndrome: (1) skull defects; (2) exophthalmos; (3) diabetes insipidus, which ultimately developed, but to wait for the detection of all these before making the diagnosis was equivalent to failing to diagnose diabetes until gangrene of the limb was seen, for Sosman, Cignolini and several others had shown that in the early days, at any rate, the condition readily responded to X-radiation.

A study of the paper by Svenningsen and of that by Frimann-Dahl on this condition in the same number of the *Acta Radiologica* would be convincing as to the importance of this early diagnosis.

No reference had been made by previous speakers to the importance of radiographs of the chests of children in cases of enlarged thymus or for the detection of opaque and non-opaque bodies in the œsophagus or bronchial tree. A discussion on such aspects would, however, require a whole evening.

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Dr. S. Vere Pearson: There are two points which I would like to make:—

(1) I am glad that Dr. Capon has mentioned the necessity for invariably studying the history, physical signs and clinical state, in conjunction with the radiological findings. About thirty years ago, at a time just before and during my post as Assistant Physician to the East London Children's Hospital, Shadwell, I used to meet, over difficult chest cases, three famous physicians of that time—Dr. Eustace Smith, Dr. J. A. Cootes and, in the summer occasionally, Dr. Jacobi (of New York). They were very keen and able. In looking back to those pre-roentgen days, it is important to realize how frequently those old gentlemen were correct in their diagnosis, as verified by post-mortem examination. There is a tendency to-day to rely upon X-rays too exclusively.

(2) I am sure I am right in recommending, especially to Dr. Shires, the taking of a second film in the case of the chests of small children, with less penetration and perhaps shorter exposure, in order to avoid missing early intrapulmonary lesions.

Section of Obstetrics and Gynæcology

President—W. BLAIR-BELL, F.C.O.G.

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Ovarian and Uterine Grafts

By Dr. MAX CHEVAL (Brussels)

ABSTRACT.—Recent experience has convinced the author of the value of ovarian grafting. He gives the histories of a number of women upon whom he made implants of their own ovarian tissue in the course of operations for double oöphorectomy. The subsequent state of these patients is contrasted with that of women after castration without grafting. When the uterus was left in position menstruation was re-established in over 80% of the grafted cases.

The author and his co-workers maintain that the vitality of autogenous grafts of ovarian substance is enhanced by hormones produced by the uterine mucosa. He therefore advocates that grafts of uterus be made in conjunction with ovarian implants whenever possible. Experiments carried out on animals have proved the correctness of this opinion.

The results of a series of cases of combined ovarian and uterine graftings are recorded, and the technique of uterine mucosa implants is described.

RÉSUMÉ.—De récentes expériences ont convaincu l'auteur de l'utilité des greffes ovariennes. Il donne les relations cliniques d'un certain nombre de femmes chez lesquelles on a pratiqué des greffes de leurs ovaires au cours d'ovariectomies doubles. L'état consécutif de ces patientes est comparé à celui des femmes castrées sans les greffes. Quand l'utérus est laissé en place, la menstruation se rétablit dans plus de 80 pour cent des cas greffés.

L'auteur et ses collaborateurs soutiennent que la vitalité des autogreffes ovariennes est favorisée par des hormones produites par la muqueuse utérine. Il recommande de faire des greffes d'utérus en même temps que les greffes ovariennes, lorsqu'on est obligé de faire une hystérectomie chez une jeune femme. Des expériences faites chez les animaux viennent à l'appui de cette opinion.

Les résultats d'une série de cas de greffe combinée d'utérus et d'ovaire sont rapportés; la technique de la greffe utérine est décrite.

ZUSAMMENFASSUNG.—Neuere Erfahrungen haben Verf. von dem Wert der Ovarialtransplantation überzeugt. Er berichtet über mehrere Fälle von doppelseitiger Oöphorektomie mit gleichzeitiger Implantation von eigenem Ovarialgewebe. Der Folgezustand dieser Patientinnen wird mit dem Zustand nach gewöhnlicher Kastration verglichen. Wenn der Uterus erhalten wurde, kam es in 80% der Fälle wieder zur Menstruation.

Verf. und seine Mitarbeiter behaupten, dass die Vitalität der autogenen Transplantate durch von der Uterusmucosa hergestellte Hormone gesteigert wird. Er meint deshalb, dass Uterusimplantation wenn möglich mit der Ovarialtransplantation kombiniert werden muss. Experimente an Tieren ausgeführt haben die Richtigkeit dieser Meinung bestätigt.

Die Erfolge einer Reihe vom kombinierten Ovarial- und Uterustransplantationen werden mitgeteilt und die Methodik der Operationen beschrieben.

IT is not necessary for me to deal at length with the importance of the ovarian graft; from the work of your President its utility has become evident. It is well known that when a woman is deprived of her ovaries she suffers from disorders at the menopause; these cannot be neglected and should, when possible, be prevented.

In this paper I shall consider only the ovarian autografts—grafts consisting of portions of the patient's own ovaries just after these have been removed. In almost every case in which diseased ovaries are removed some fragments can be found sufficiently healthy to be worth transplanting. These preserve the ovarian function for a period that I cannot yet determine, my research being of too recent date.

It was in September 1932 that I first became interested in this question. I knew from the work of Professor Blair-Bell that when the uterus is preserved the menstrual function persists for years if autografts of the ovaries are implanted.

I must apologize for apparently failing to give due recognition to previous workers in this field. The subject is too wide to be adequately considered in this paper, but it is clear from the literature that ovarian autografts are of undoubted value when the uterus, or at least a portion of it, can be retained.

I wondered whether it would be useful to perform ovarian transplantations during the process of removal of the uterus, and I considered whether, if degenerative changes appeared in the ovarian grafts as the result of hysterectomy, there might perhaps be a means of lessening their severity, if of not entirely preventing them, by performing uterine grafts.

It is from this aspect that I have envisaged the problem since October 1932. Since then I have studied it by means of animal experimentation, and at the same time I have been using the method in my gynæcological operations.

Experiments

In conjunction with Charles Mayer, I have made all my experiments on dogs. In the first series we performed double ovariectomies and grafted half of each of the ovaries into the rectus abdominis, following the procedure of Blair-Bell.

In the second series we removed the whole uterus, including the cervix and tubes, in addition to both ovaries. Thus we performed total hysterectomies, and grafted half of each of the ovaries into the rectus abdominis.

In the third series we performed the same operation as in the second, but in addition on each occasion we grafted two considerable portions of the uterine cornua into the subcutaneous cellular tissue.

Series I.—*Uterus left in situ. Intramuscular ovarian grafts.*

When an ovarian graft is examined it is seen that the ovary has undergone profound changes ; these were manifest in all our experiments.

The centre of the ovarian fragment undergoes a colloid sclerosis of the connective tissue, and it is only at the edges of the graft in contact with the nourishing tissue that the ovarian elements are recognizable ; they are composed of primordial follicles the number of which depends on the state of the grafted ovary and on the time at which the graft is examined. Together with these primordial follicles, there are found a greater or less number of follicles whose oöcyte has degenerated. Intermediate stages are seen between the primordial follicles and these small cavities which are surrounded by granular cells. In some places the germinal epithelium disappears, so that there is direct contact between the tissue of the bed of the graft and the superficial connective tissue of the ovary. In other places the germinal epithelium proliferates, forming several layers of cells between which cystic cavities of small dimensions are frequently produced. In certain places the germinal epithelium forms solid or hollow cords which penetrate to a variable depth into the ovarian tissue. This process, which exists normally in the dog, is often met with in our grafts.

As to the maturing ovarian follicles which we came across in the fragments of the ovary collected as controls at the time of operation, they disappear in the grafts ; as a rule, after fifteen days we only found very small traces of them—merely more or less rounded empty cavities, sometimes containing granular cellular débris. Similarly, the luteal formations undergo a rapid degeneration and, after fifteen days, they consist of connective tissue fibrils between which one recognizes here and there a few degenerate luteal cells.

The first examination shows that all the maturing follicles and the corpora lutea disappear from the graft and that there is left only a thin layer of ovarian tissue on the surface of the graft. This tissue contains primordial follicles, with or without oöcytes, and some germinal epithelium.

I will now describe the results of our first series of experiments. The practice of ovarian autografting prevents the uterine atrophy which usually follows a double

oöphorectomy—a fact agreed upon by the numerous authors who have studied this question.

(1) *After fifteen days.*—In the centre of the graft there are a few remaining traces of the developed elements which were present in the ovary at the time of implantation (follicles more or less ripe and corpora lutea which are in course of degeneration).

The periphery of the grafts is composed of a crown of primordial follicles most of which have kept their oöcytes intact.

The germinal epithelium is found in some places; it is formed of several cellular layers between which small cystic cavities are occasionally to be found.

(2) *After one month.*—Few traces of the developed ovarian elements are found; the ripe follicles and corpora lutea have completely degenerated and have been absorbed. The periphery of the graft is composed of primordial follicles and germinal epithelium. Tubes of Pflüger, solid or hollow, branch off from the latter (fig. 1, Plate I).

(3) *After three months.*—Sometimes traces of old luteal formations are found, completely degenerated. The layer of primordial follicles is well preserved; some follicles show the beginning of maturation which may be recognized by the cylindrical character of the granular cells and their double stratification (fig. 2, Plate I). A few follicles undergo granular atresia; the ovule has disappeared; granular cells are developing, stretching, and forming a series of cylindrical nucleated cells which are packed one against another in a palisade formation. The thecæ which surround them show no visible hypertrophy. This form of atresia exists normally in the ovary of the dog. We seldom meet it in our preparations from animals in which the uterus has been retained. The germinal epithelium, which in many places has disappeared, gives rise in certain situations to epithelial formations arranged in tubes of variable diameter, often set parallel to the surface of the ovary.

(4) *After four months.*—The presence of numerous follicles—from primordial follicles to those in process of maturation—is to be observed. We have not, however, in our preparations, discovered follicles containing fluid. The phenomena of maturation have not yet reached this stage. The interfollicular stroma is occupied by numerous epithelioid cells forming the interstitial gland. Finally, the germinal epithelium persists in places and reacts in the usual way, giving rise to fairly numerous tubes of Pflüger, both solid and hollow.

Discussion of results.—(i) The superficial portion of the ovary is the only part of interest from the point of view of the graft, inasmuch as it contains the primordial follicles, the only elements which have enough vitality to make the graft successful. In fact the more highly developed elements degenerate, owing either to trophic disturbances or to a peculiar fragility resulting from their differentiation. It is only three or four months after grafting that the primordial follicles once more begin to mature; it is necessary to wait for this period before ovarian activity is renewed.

(ii) The germinal epithelium forms no obstacle to the success of the graft; its extreme fragility causes it to disappear from the greater part of the surface of the graft as a result of the manipulations it undergoes at the time of the cutting of the graft and of the reaction of the graft-bed on the graft itself. It persists in parts, however, forming a multistratified layer in which small cystic formations occur. It gives rise to the tubular epithelial formations which we have noticed.

Series II.—Ovarian autografts after bilateral ovariectomy and total hysterectomy.

The modifications reported in this series are independent of any ovarian vascular disturbance which might result from hysterectomy, as the ovaries grafted after hysterectomy are compared with the grafts in the preceding series in which the uterus was preserved intact.

In this series we removed the uterine cornua, the cervix, and the whole of the Fallopian tubes, including the fimbriæ. It was difficult in these animals to distinguish where the body of the uterus began and where the tubes ended. Some

authors, in order not to disturb the circulation of the ovaries, which have been left in position, do not remove the tubes. I believe that this is an error which in all probability explains the differences in the results obtained. Our procedure was total hysterectomy and at each autopsy we made sure that neither tubes nor uterine cornua—nor even cervix—remained.

After hysterectomy the ovarian grafts show signs of a central sclerosis, only the periphery of the ovary having survived. They consist of a more or less extensive crown of primordial follicles and of germinal epithelium in some places preserved and in others having disappeared.

(1) *After fifteen days.*—On the surface of the grafts there is the usual reaction of the germinal epithelium which is hypertrophied in some parts and is composed of several cellular layers between which small cavities are formed. In other places the germinal epithelium has disappeared. Again, we meet with primordial follicles and some anovular follicles. But what is particularly striking are the phenomena of hypertrophic atresia which are produced in relation to certain of the follicles. The ovule disappears, the granular cells hypertrophy displaying numerous karyokineses and becoming differentiated from the thecal cells which in some places penetrate as intrusions between the granular formations. These thecal cells themselves undergo a certain amount of hypertrophy.

(2) *After one month.* Appearances are observed in every particular identical with those of fifteen days.

(3) *After three months.*—The graft shows important tubular formations produced by the germinal epithelium. They penetrate it deeply, and in the sections the appearances of anovular follicles are very well shown. In the wall of some of these formations certain cells are differentiated and give rise to newly formed ovules. Again, there are found in the graft, in two places, clear evidence of characteristic atresia of the follicles (fig. 3, Plate II). Nowhere do we find follicles in process of ripening, but numerous primordial follicles are to be seen in our sections. Some of them appear to be follicles which have survived in the graft but others may be interpreted as being newly formed follicles (fig. 4, Plate II).

(4) *After four months.*—The two grafts removed from the dog operated on four months previously consist of numerous cysts, irregular in shape, containing a large quantity of clear liquid. Between the cysts there exist bands of well-preserved ovarian tissue ; the ovaries have not altogether degenerated. The usual forms of germinal epithelium are found with well-developed egg-tubes (Pflüger) both solid and hollow. In some of these epithelial strands are newly formed ovules similar to those which were found after three months. The bands of ovarian tissue are filled with numerous follicles in all stages of maturation—primordial follicles, follicles in process of maturation, and ripe follicles containing a large quantity of fluid. Few atresic follicles are to be seen. In certain multi-ovular follicles two of the ovules are reaching a state of atresia while the third still has a normal histological appearance. In some other follicles the ovule has disappeared and atresia such as that described above has occurred.

(5) *After six months.* The appearances confirm the previous statement, that as a result of hysterectomy, the ovarian graft has lost, owing to atresia, a large number of follicles. The follicles which have remained intact however follow their normal course of evolution. Some are ruptured on ripening, and we verify in our grafts of six months recent luteal formations which are evidence of the resumption of ovarian function.

Discussion of results.—(i) After hysterectomy in the dog marked follicular degeneration takes place : in making this statement I am in agreement with several authors—among them Fellner, Henkel, Jakobsohn, Lindig, Takakusu, Zimmerman, Parfenoff, Watrin and Brabant, Sessums and Murphy. In the follicles, atresia occurred ; this also has been observed by many authors.

(ii) I wish to emphasize the fact that the grafts do not die, and that after six months there are still found in them intact follicles, some of which are in process of normal maturation.

(iii) The germinal epithelium reacts strongly, giving rise to hollow or solid strands which penetrate the cortex of the graft. In the wall of some of these are newly formed ovules. This condition is frequently found after total hysterectomy, but has rarely been seen in our other experiments with ovarian grafts. This phenomenon appears to be of a compensatory nature tending to make up for the loss of ovules which has resulted from the hysterectomy.

Series III.—*Uterine and ovarian autografts after bilateral ovariectomy and total hysterectomy.*

The procedure here consists in splitting the cornua as soon as they have been removed by total hysterectomy, on the side opposite the broad ligament. They are held open between two pressure forceps, the peritoneal side is scraped with a bistoury in order slightly to reduce the quantity of uterine muscle to be grafted and to allow for a better vascularization of the intact mucous and submucous tissue. The middle portion, forming a flattened ribbon from 2 cm. to 5 cm. long, is then placed, with the mucous membrane uppermost, in the subcutaneous cellular tissue outside the laparotomy wound.

The dogs were killed respectively fifteen days, one month, four months, and six months after operation.

(1) *After fifteen days.* The sections show a large number of places in which the mucous membrane has degenerated, forming amorphous masses, staining deeply with hæmatoxylin and still having the general character of the uterine villi. They are surrounded by uterine muscle more or less well preserved. In other parts, however, which themselves are vascularized and have once more become active, there are uterine glands with their mucous membrane the cylindrical epithelium of which in some places shows karyokinesis. The lumen of some of the glands is filled with abundant mucus. The uterine muscle is very clear, the muscle cells having a parallel fusiform structure and their nuclei being well stained (fig. 5, Plate III). The uterine muscle seems to have suffered less than the mucous cells as the result of grafting.

(2) *After one month.*—The preparations show in many places that the mucous membrane has undergone extensive degeneration, but where the glands have developed they form cystic cavities edged with an epithelium which becomes flatter as the cyst becomes more voluminous. In some places the cystic cavities have lost their epithelium, this having disintegrated (fig. 6, Plate III). However, in all these preparations there are still well-formed uterine glands containing little or no mucus, showing that the mucous tissue of the whole graft is far from being completely destroyed.

(3) *After four months.*—The uterine graft has adapted itself to its new position. There are no longer any traces of necrosed portions and cystic areas: these having been reabsorbed. The centre of the graft is occupied by a star-shaped cavity running through its whole length. This cavity is lined with uterine mucous membrane of perfectly normal appearance (fig. 7, Plate IV). The cells of the cylindro-cubical epithelium clearly show karyokinesis (fig. 8, Plate V). The uterine glands penetrate into the depths of the mucous membrane until they reach the uterine muscle. They contain very little mucus. Everything occurs as though the external secretion of these glands had ceased. The interglandular connective tissue has the usual appearance of the connective tissue of the uterine mucosa. The muscle fibres retain the characters recorded on the fifteenth day.

(4) *After six months.*—The grafts retain the same appearance as after four months, with the sole difference that the phenomena of repair are concluded, and there are only a few karyokinetic figures to be seen in the epithelium of the uterine mucosa.

In the dogs in which grafting of fragments of the uterus was performed after total hysterectomy we proceeded to double ovariectomy, and grafted half of each ovary into the rectus abdominis.

(5) *After one month.*—The grafts are well preserved, and contain numerous follicles with their oöcytes. Some of them already show signs of maturation, namely, increased volume of the cells of the granular layer, and a tendency towards double stratification. At the same time, in a few follicles changes of atresia are produced, but the thecal cells participate very markedly in the changes (fig. 9, Plate V). The granular cells have almost disappeared, and are replaced by the bulky thecal cells which display a luteal reaction characterized by the formation of lobules composed of cells with spongy cytoplasm whose meshes are filled with lutein. The nuclei are plainly visible and well stained. In other grafts this luteinization is less noticeable, but nevertheless wherever an atresic follicle is met with, the thecal cells manifest this reaction in an unmistakable way. The germinal epithelium shows numerous thickenings, with formations of a great number of tubes of Pflüger which penetrate the underlying tissue.

(6) *After three months.*—The grafts show well-formed follicles with their oöcytes. Some of these follicles are surrounded by granular tissue with large many-layered, mitotic cells, thus giving evidence of the beginning of maturation. There is little follicular atresia, but when any is present there is a definite tendency to luteinization of the thecal cells. Lastly, the germinal epithelium displays its characteristic reaction; that is to say, multistratification and penetration of the ovarian tissue in the form of the tubes of Pflüger.

(7) *After four months.*—The grafts do not show the cystic degeneration that was found four months after hysterectomy performed without uterine grafting. Follicular atresia is very rare. When it does occur it is accompanied by a pronounced reaction of the thecal cells, with a tendency to luteinization, and even by the formation of true corpora lutea. As for the follicles, they are found in all stages of development—primordial follicles, follicles with many-layered granular tissue, and follicles almost ripe, containing a large quantity of fluid in which floats, almost free, an ovule with a perfectly staining nucleus, surrounded by its crown of granular cells, and the germinal epithelium forms numerous tubes of Pflüger which penetrate deeply into the ovarian tissue.

(8) *After six months.*—The grafts show unmistakable signs of activity. One finds ripening follicles and corpora lutea resulting from the recent rupture of ripe follicles. What is most remarkable of all, however, is that there is no longer any reaction of luteinization in the thecal cells of the follicles.

Discussion of results.—(i) The uterine fragment is easily grafted into the subcutaneous cellular tissue. At first it produces a disturbance of the epithelial cells of the mucous membrane and of the glands, accompanied by a copious production of mucus. The result of this is the formation of mucous cysts bringing about degeneration of the epithelium which desquamates. At the fourth month this reaction has ended, a more or less regular uterine cavity is formed, lined with an epithelium from which uterine glands break off which scarcely secrete any mucus. After six months the graft assumes an appearance which appears to undergo little change for a very long time.

(ii) The ovaries display intact primordial follicles; there is rarely any follicular atresia, and when it occurs it is accompanied by luteinization of the thecal cells, often very marked, giving place to the characteristic appearances of corpora lutea. The cause of this luteinization is problematical. The experiments of Loeb on pseudo-gestation may offer some explanation, as we have been able to reproduce this phenomenon in the dog. The experiment is as follows: The two ovaries are removed and half of each of them is grafted into the rectus abdominis muscle. The uterus is left in situ and we affix a large silk thread to each of the uterine cornua in order to produce Loeb's decidual reaction. When the grafts are examined after a month they are seen to be filled with follicles whose thecal cells have undergone luteinization. What happens when the uterus is grafted? During the first month an active absorption of uterine tissue takes place, in consequence of which the blood

of the animal contains an excessive amount of uterine hormone and as a result of this the luteal reaction of Loeb occurs. Towards the fourth month this luteal reaction is still apparent; towards the sixth month it no longer exists because the resorption of the uterus is complete, the graft having reached the final stage of organization.

Clinical Observations

In collaboration with Leopold Mayer and Leo Dejardin I have studied what occurs in women. I am not now dealing with those patients on whom we have operated for retroversion, pedunculated fibroma, etc., and in whom the reproductive function has been preserved. In common with all gynæcologists we have been bound to conserve this function whenever possible but with these cases the present paper is not concerned.

From October 1, 1932, to February 1, 1934, we have had to terminate the reproductive function in 56 women. In one case the ovaries were in such a bad condition that we could find no ovarian substance to graft; in another there was such a severe inflammatory condition that we were unable to graft fragments of the ovaries; in two others, in which the patients were over 50, grafting was not performed. In the remaining 52 cases we were able to perform grafting. That is to say that this method can be used, if desired, in almost every case of operation. These figures indicate the remarkable progress made since October 1932. Before that date these 52 women would all have been sterilized or would have retained in the peritoneal cavity ovaries which might subsequently have undergone pathological changes necessitating a further laparotomy.

When it is impossible to preserve the reproductive function in our patients we prefer, as a rule, to transplant the ovary alone, if the uterus is healthy and can be left in situ. But when it is necessary to remove the uterus also, we graft strips of uterine mucosa, in addition to fragments of ovary, unless this procedure is contra-indicated by infection of the excised uterus or its appendages.

In eight cases we performed "homografts," that is to say transplantations from one woman to another, but as yet our experiments have been too few to allow of our forming any opinion on this complex problem.

The patients who underwent double salpingo-oöphorectomy, with retention of the whole uterus in situ and ovarian autografting, usually menstruated normally four months after operation. We have performed this operation twenty-five times, twenty of which were more than four months ago. Sixteen of these twenty patients have menstruated (four have not yet been seen again). It is therefore no exaggeration to say that we have obtained a positive result in over 80% of our cases.

We have carried out six removals of the uterine fundus followed by ovarian autografting; five of these were more than four months ago: in four of these five cases the patients have menstruated. In five of the cases in which we performed hysterectomy we used ovarian autografts only. No symptoms have been complained of and three of the patients have had no menopausal trouble. Finally, in eight cases we implanted uterine and ovarian grafts after hysterectomy. As we are the first to have performed subcutaneous uterine grafts in women, we will describe the technique.

After direct examination we remove the healthier ovary. We cut grafts from this and plant them in the rectus abdominis, as described above. We next perform hysterectomy. The excised uterus is divided along its lateral borders and across the fundus by means of a strong pair of scissors; it is thus separated into anterior and posterior halves. These are placed on sterile compresses, the triangle of the uterine mucous membrane being upwards, and each half is soaked in a 5% tincture of iodine. The operator then changes his gloves and cuts, with a sterile bistoury, a slice composed of mucous and submucous coats and a small amount of uterine muscle. The fragments thus cut off may best be compared to a coin. A cutaneous incision of a few centimetres is made into the abdominal wall well outside the laparotomy wound. With a Kocher's sound a space is formed in the subcutaneous

adipose tissue and the graft is implanted in it. Several clips close the skin incision. Sometimes after from eight to ten days the grafts showed signs of slight fluctuation and on two occasions we pierced them with a large hollow needle mounted on a syringe but we could never aspirate the slightest trace of serous fluid and in the end everything settled down. The later operative results have always been equally uncomplicated. During the first four or five months following operation the patients complained of menopausal disturbances; in six of these cases, operated on more than four months ago, these subjective symptoms decreased in severity and rapidly disappeared.

In two of these six cases the details are particularly interesting:—

In one case the uterine implant was removed six months after the operation. The patient, aged 34, was operated on for fibroma of the uterus on December 10, 1932. The position of the fibromatous nodules was such that we gave up the idea of preserving the uterus, even partially. The left ovary was removed and we cut grafts from it and implanted them in the superficial part of the rectus abdominis under the aponeurosis. The uterus and the adnexæ were removed by low subtotal hysterectomy. A graft of mucous membrane the size of a florin was placed in the subcutaneous cellular tissue at the level of the left anterior iliac spine. The wound healed by first intention in fifteen days. For three months this patient complained of menopausal disturbances which afterwards decreased. Between the fourth and fifth month following operation congestion of the uterine graft was apparent on palpation. This phenomenon was manifested again in the course of the fifth and sixth months. The patient, an extremely neurotic woman, was anxious about her symptoms and we decided, as a matter of scientific interest, to remove the uterine graft. This we effected, very easily, on June 16, 1933, under local anæsthesia. The fragment of mucous membrane had existed for six months and six days in the subcutaneous cellular tissue. It had the form of a cylinder, 4 cm. long and ½ cm. in diameter, rounded at both ends. On section it was found that a cavity extended almost the whole length of the cylinder. This appeared to be entirely closed and contained a thickish but clear liquid. Microscopic sections were cut at different levels and all showed similar appearances. The graft appeared to bend in the direction of one diameter, the mucous membrane inside, the masculature in a horse-shoe outside, not completely surrounding it. The cavity was lined with uterine mucous membrane, perfectly preserved, composed of definite cylindro-cubical cells with clearly defined nuclei. Karyokinesis was well marked in this epithelium. A large number of glands penetrated the depth of the mucous membrane up to the junction with the uterine muscle. The connective tissue of the mucous membrane presented the usual appearance of normal interglandular tissue at the intermenstrual stage (fig. 10, Plate VI). In the glandular cavities and in the newly found uterine cavity there was a little clear mucous secretion in which desquamated cells were found, a few white corpuscles and a good many red corpuscles. The latter were also met with in the intercellular spaces of the superficial part of the mucous membrane (fig. 11, Plate VI).

The uterine muscle had retained its normal characters—bundles of parallel fusiform cells with well-stained nuclei. In the subcutaneous connective tissue and in the connective tissue adjacent to the graft, particularly at the level of the muscular horse-shoe opening, were found numerous collections of macrophages full of hæmosiderin, a proof that hæmorrhage must have occurred recently and be in process of resorption. This observation proved indubitably that after six months the uterine graft was in excellent condition and that it had been the site of a recent hæmorrhage. Thus we obtained by the uterine graft the formation of a small endometrioma which both clinically and microscopically had been the site of menstrual changes.

The history of our earliest case is as follows:—

On December 3, 1932, we performed hysterectomy on a young woman aged 26 years and 6 months, on account of uterine fibromatosis which did not permit preservation of the uterus. We implanted an ovarian graft in the rectus abdominis, according to the technique of Blair-Bell, and we grafted a fragment of the uterus into the subcutaneous cellular tissue. When seen on February 9, 1934, the patient complained of pains in the region of the uterine graft; these appeared at more or less regular intervals, and were accompanied by a livid tint in the wound. The graft, implanted very superficially and immediately beneath the skin. was easily felt in the form of a small cylinder 4 cm. long and 1 cm. in diameter. It is probable that the slight pains noticed by the patient occurred at the time of the menstrual period and that the latter was possibly manifested by slight ecchymosis under the skin. This patient has no menopausal disturbance and the grafts are functioning, fourteen months after operation.

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PLATE I

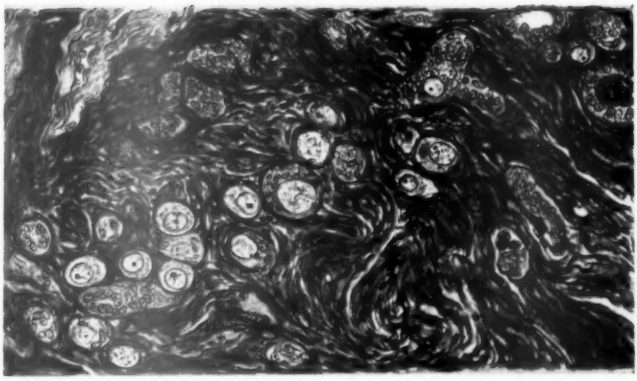

FIG. 1.—Ovarian graft of thirty days. (Uterus left in situ.) Formations of germinal epithelium, primordial follicles, and anovular follicles (Oc. 5, obj. 5).

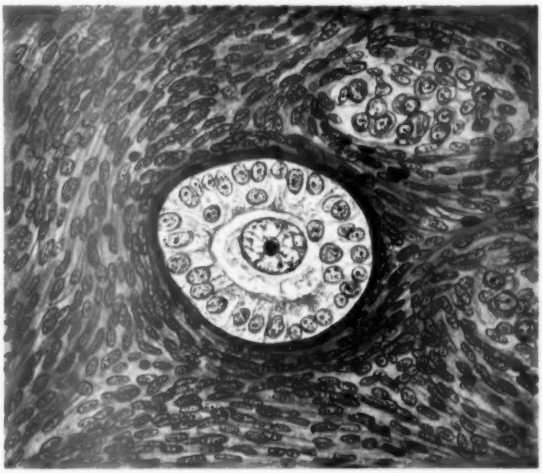

FIG. 2.—Ovarian graft of three months. (Uterus left in situ.) Follicle in process of maturation (Oc. 5, obj. 7).

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PLATE II

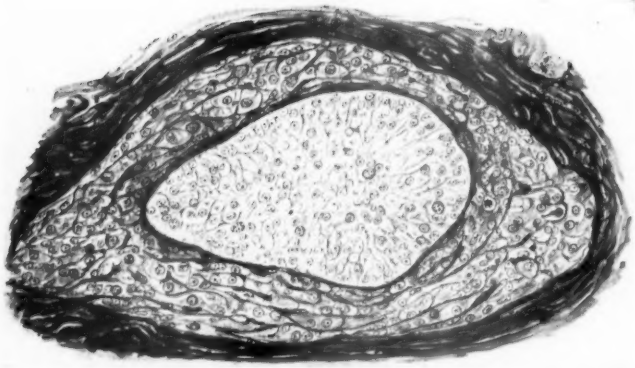

FIG. 3.—Ovarian graft of three months, after hysterectomy. Follicular atresia (Oc. 5, obj. 5).

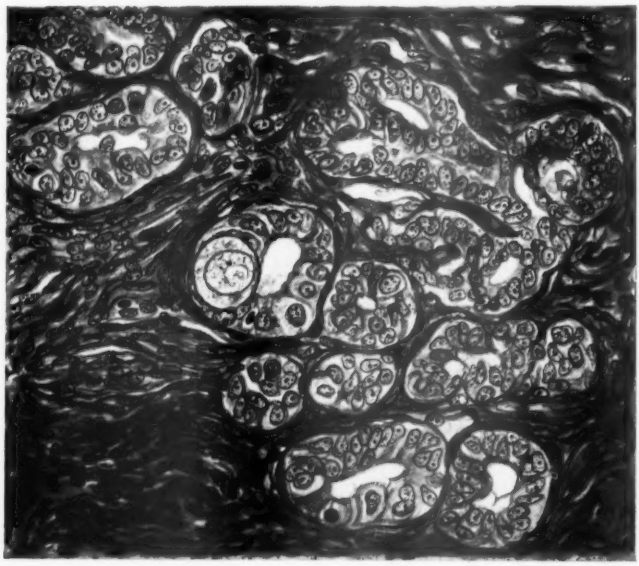

FIG. 4.—Ovarian graft of three months, after hysterectomy. Ovular neoformation at the expense of a tube of Pflüger (Oc. 5, obj. 7).

PLATE III

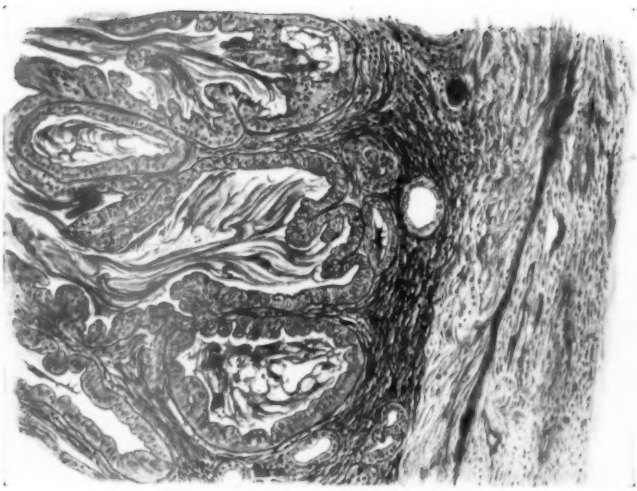

FIG. 5.—Uterine graft of fifteen days. On the left, uterine glands containing mucus; on the right, uterine muscle (Oc. 5, obj. 5).

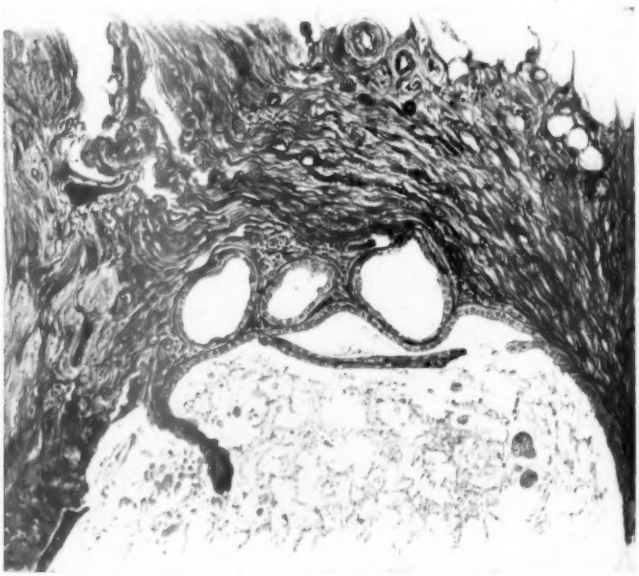

FIG. 6.—Uterine graft of one month. Cystic degeneration of some of the uterine glands (Oc. 5, obj. 5).

PLATE IV

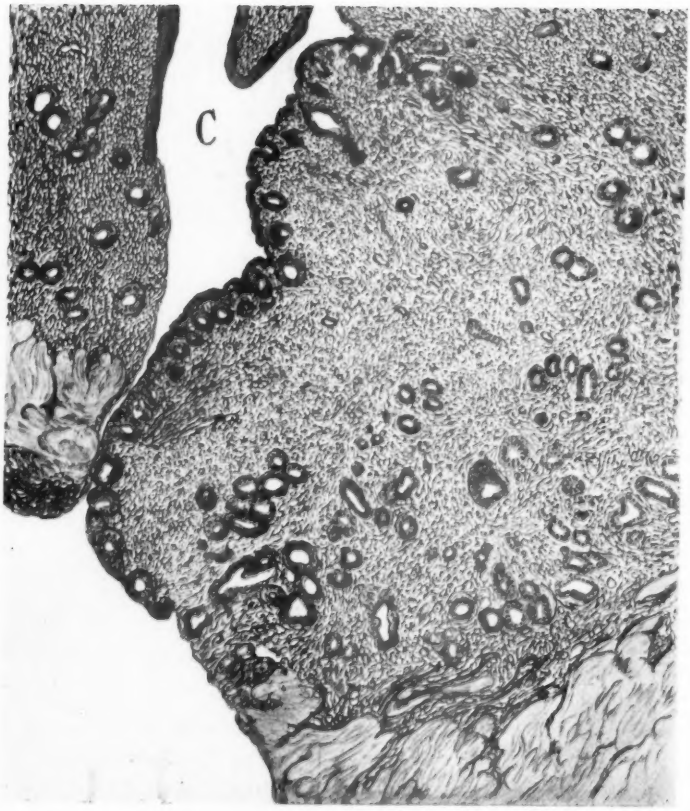

FIG. 7.—Uterine graft of four months. (C) Uterine cavity. Uterine muscle below; mucous membrane with its glands between the two (Oc. 5, obj. 3).

PLATE V

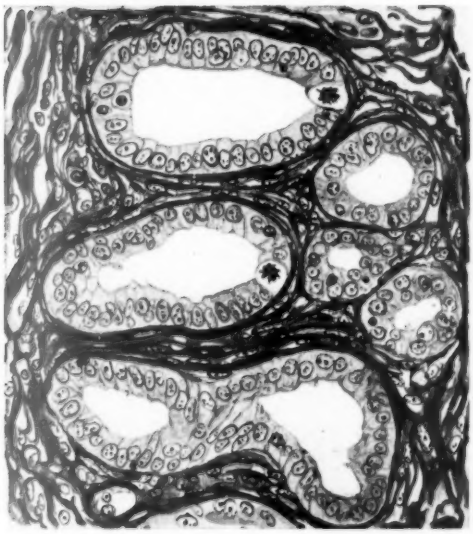

FIG. 8.—Uterine graft of four months. Glands of the mucous membrane highly magnified (Oc. 5, obj. 7).

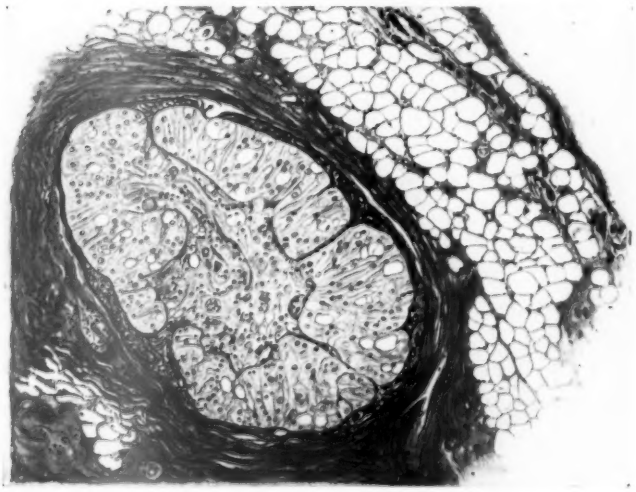

FIG. 9.—Ovarian graft of thirty days, after uterine grafting. Complete luteinization of a follicle (Oc. 5, obj. 5).

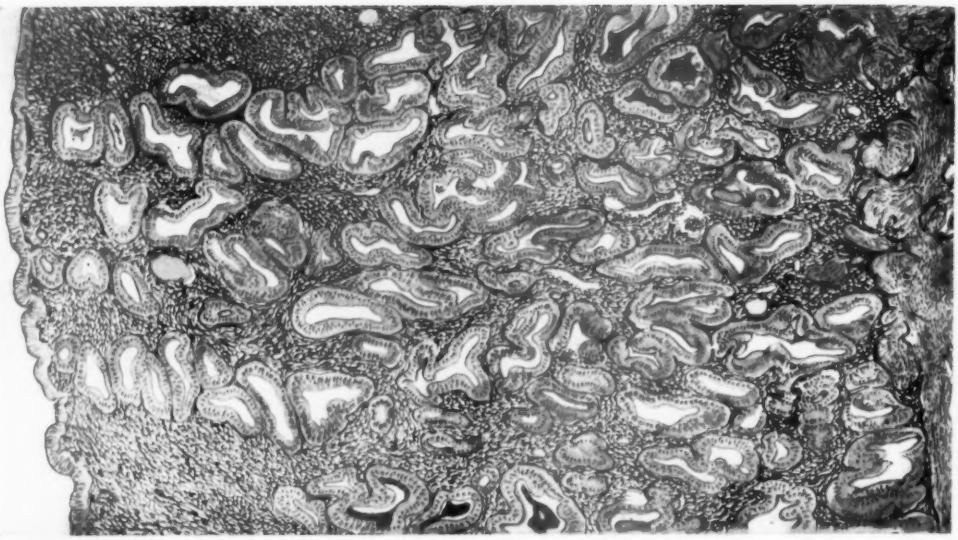

FIG. 10.—Uterine graft of six months in a woman On the left, uterine cavity, on the right, uterine muscle; mucous membrane at the intermenstrual stage between the two (Oc. 5, obj. 3).

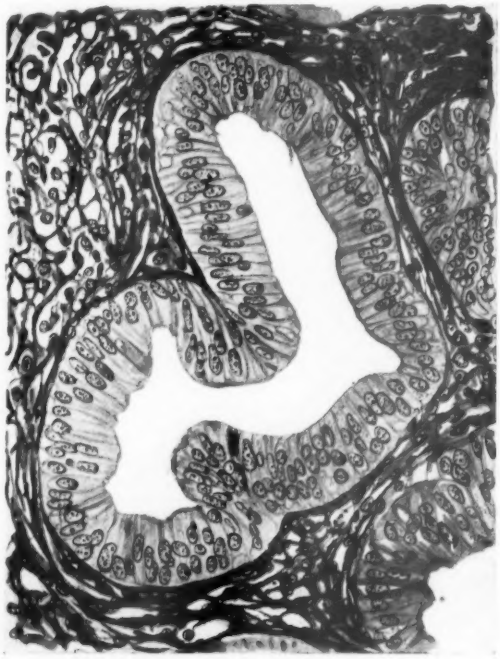

FIG. 11.—Uterine graft of six months in a woman. Gland of the mucous membrane, highly magnified (Oc. 5, obj. 7).

SUMMARY

I will now summarize my present views on the subjects I have discussed, but my experience is too recent for me to presume to give a final opinion.

(1) The ovarian autograft should be used in almost all double oöphorectomies. It is particularly important to graft fragments of the superficial part of the ovary and to avoid handling them in such a way as to destroy the germinal epithelium and the subjacent layers of primordial follicles. Intramuscular and even subcutaneous ovarian grafts are successful in all cases operated on aseptically. Provided that the grafts are composed of sufficiently healthy tissue, the ovarian hormone proportion in the organism is maintained at a normal level.

(2) The uterine autograft is easily effected in subcutaneous cellular tissue. At first, experimentally, intense resorption of uterine products is established and is explained by a luteal change of the ovaries. Later, the small endometrioma adapts itself to its new position and, more than a year afterwards, displays indubitable signs of vitality.

(3) Grafts of ovaries in hysterectomized dogs exhibit phenomena of follicular atresia, sometimes cystic. After six months fewer follicles remain but some are met with which are clearly about to mature.

(4) Ovarian grafts performed after hysterectomy and uterine grafts show a small degree of atresia. After six months both grafts show very plain signs of activity.

In women hysterectomized under 40 years of age uterine grafting should be performed whenever possible, in order to maintain a stronger vitality of the ovarian grafts. Between the ages of 40 and 50 ovarian grafting alone should be used. In women aged over 50, grafts are useless.

Discussion.—Dr. HERBERT SPENCER said that the subject of hormones was one of the most fascinating in modern medicine, and that of the gonadal hormones especially so. In this study the President had taken an important part. The Aschheim-Zondek reaction and its modification by a Belgian lady, Adèle Brouha, had furnished a method of diagnosing pregnancy, which was of the highest importance. With regard to ovarian and uterine grafts, he had certain reservations. It was well known that ovarian grafts maintained the menstrual function in the patient, but they involved an operation and merely postponed the menopause. Many patients suffered very little inconvenience after total removal of the uterus and ovaries. He (Dr. Spencer) had been accustomed to leave one ovary—or a portion of one ovary—when performing hysterectomy on account of myoma. But in three such cases malignant disease had subsequently developed in the ovary not removed; in one case a sarcoma had developed in the ovary thirteen years after the removal of the uterus. He had regretted that he had not in these cases removed both ovaries, and he thought that similar regret would be felt by the operator who inserted grafts, if these subsequently became infected or developed malignancy. It must, however, be admitted that most of the patients in whom an ovary or part of an ovary had been left, continued to have perfect health, although no uterine tissue remained.

With regard to uterine grafts, it was certain that they produced an endometrioma, which was sometimes painful, and the sterility of the uterine graft was not so easy to obtain as in the case of the ovary.

The vast amount of research on the ovarian hormones led one to hope that synthetic hormones would be produced which would be effective when administered by the mouth or by suppository.

Dame LOUISE MCILROY said that she had carried out a considerable number of ovarian graft operations on rabbits, and had found that the results were more comparable with the human when monkeys were employed. Some of these latter animals she kept for a year after the operation. The grafts were implanted either in the abdominal wall or in the broad ligament after oöphorectomy had been performed. The grafts grew and no atrophic changes took place in the uterus or vagina. She had performed the operation several times in women with degeneration of the ovaries, but she had given up the operation as she could see little necessity for it. The smallest piece of ovary that could be used for a graft elsewhere was very much better left in its original situation, as there was no interference with the nerve or blood-supply, and hypertrophy of the fragment usually occurred with the maintenance of normal function. In a few of such cases she had had experience of a subsequent pregnancy following.

She could see the advantage of implanting ovarian grafts from other individuals, but she had had no experience of this operation.

This was the first time that she had been made aware of the utility of uterine grafts. Most gynæcologists, however, had experience of the disadvantages of endometriomatous rests. Was it not possible that some uterine grafts might display such changes? Was it to be understood that the growth of the uterine graft was dependent upon the growth of the ovarian graft?

There was no doubt that the high-up operation—supravaginal hysterectomy—was desirable when the ovaries were normal, as it allowed for much better excretion. Conservative methods such as these had points in their favour in spite of the warnings put forward by those who advocated panhysterectomy in case subsequent cancer might develop.

The PRESIDENT said that he himself had done much experimental work on this subject, the results of which were summarized in his book "The Sex-Complex," and he had practised this procedure in the human subject 218 times, the first operation being performed in 1912, and 214 between 1916 and 1931. Ovarian grafting had, however, been sadly neglected by gynæcologists in Great Britain.

The principles on which it was based were the following:—

(1) It was an essential principle of surgery that only those structures should be removed which were diseased beyond hope of recovery or were a source of danger to the patient, conservation of function being obtained whenever possible. The eradication of ovarian tissue without proper cause was, therefore, bad surgery, for the ovaries were of metabolic and psychological value to the patient.

(2) Clinical as well as experimental investigations had shown that ovarian grafting was practicable.

With regard to the clinical aspects, he recalled a statement which he had made in concluding his first paper on the subject in 1920: "I wish again to insist that this procedure be looked upon as a measure of necessity which can never be weighed in the balance against the preservation of the natural connexions in the normal ovary." He had never swerved from that restriction, hence the number of his cases was not so large as otherwise it might have been.

It followed, then, that in salpingitis—the chief indication for ovarian grafting—the ovaries should be removed only when the tubes—especially pyosalpinges—could not be excised without the blood-supply to the ovaries being impaired. Again, with neoplasms it was often possible to preserve unaffected a portion of the ovary with its blood-supply, for innocent tumours tended to grow away from the hilum.

With regard to the technique of the operation, the points of importance seemed to be the following:—

(*a*) Autoplastic grafts only should be used.

(*b*) The portion of the ovary to be grafted should be attached immediately to a long ligature and dropped into the pouch of Douglas, or elsewhere in the peritoneal cavity, until required, in order that it might be kept warm and moist.

(*c*) The graft should be rendered amenable to rapid vascularization. He himself preferred to remove most of the dense capsule of the human ovary (tunica albuginea). It was unnecessary to preserve the superficial follicles which were liable to become cystic, as had been recorded by himself and others, for he had shown that in the rabbit the interstitial cells alone were sufficient to keep the uterus functional, and this observation was supported by the work of Parkes and others on X-ray destruction of the follicles. The material to be used was then sliced in a criss-cross fashion, without detachment of the fragments, on a rubber pad. He thought this better than employing a number of separate grafts in different sites.

(*d*) A vascular site for the nidus should be chosen. He had generally implanted the graft in a blood-free nidus among the fibres of the right rectus abdominis. He had, however, sometimes placed the graft into the uterine wall—when the surface could be left undenuded and exposed—and once or twice in the omentum.

The following table gave an analysis of the indications and results in 218 cases:—

Ovarian Grafting in the Human Subject

I. Total number of cases recorded 218

II. Ages of the patients:

		Number		Average age
17-30 (inclusive)	...	106	...	24·8
31-40 „	...	90	...	35·4
41-47 „	...	22	...	42·7
17-47 „	...	218	...	31·0

III. Indications for operation :

A. Salpingitis				201
(*a*) Primary lesion (including 6 cases of recent puerperal infection)		182		
(*b*) Associated with appendicitis		4		
(*c*) ,, ,, fibromyoma uteri		14		
(*d*) ,, ,, tubal gestation		1		
B. Innocent neoplasms of the ovaries				16
Endometriomata		4		
Other neoplasms of both ovaries, or of a remaining ovary ...		12		
C. Ovarian pain with functionless uterus				1
IV. Total number of cases excluded				84
(*a*) Deaths after operation		5 (2·2%)		
(*b*) After-histories, or after-histories extending over six months, not obtained		79		
V. Total number of cases analysed				134
A. Number of cases in which menstruation was possible ...		113		
(*a*) Number of cases in which menstruation occurred	80 (70%)*			
(*b*) Number in which menstruation was absent, but the menopause was averted	14*			
(*c*) Number in which menstruation was absent and menopausal symptoms occurred	19			
(i) Very slight and initial ...	(15)*			
(ii) Well-defined menopause ...	(4)			
B. Number of cases in which menstruation was impossible (hysterectomy) ...				21
(*a*) Number without menopausal symptoms after initial disturbance	14*			
(*b*) Number in which the menopause occurred ...	7			
C. *Functional results obtained			123	(91%)

It would be seen that functional results were obtained in 91% of the cases, and that when menstruation was possible this had occurred in 70%. Ovarian grafting itself should not cause a fatality. The mortality rate shown (2·2%) was satisfactory in view of the serious nature of some of the lesions.

With regard to the character of menstruation following ovarian grafting, it was first to be noted that the patient usually, but not always, had menopausal symptoms for a few months after the operation. This was evidence of the complete removal of ovarian tissue from its normal site, for until vascularization of the graft was well established the ovarian secretions were not fully available. Sometimes, however, the subsequent onset of menstruation was not long—if at all—delayed, possibly owing to immediate absorption of secretion already formed in the grafted tissue. Nevertheless, in such circumstances a fragment—an unintentional graft—might have been left in the pelvis. This had occurred, so far as he knew, in only one of his cases, in which a small cyst formed at the back of the broad ligament. This was removed and menstruation continued from the graft in the rectus muscle.

In some cases menstruation occurred at longer intervals than normal, and ceased a year or two later. In these women the menopausal symptoms were mild. On the other hand, menstruation might continue normally for many years. Two days ago he had received a letter from a patient, now resident in London, on whom he had operated in December 1918 when she was aged 24. It was a serious case of salpingitis in which drainage was employed. Acrohysterectomy with bilateral salpingo-oöphorectomy was performed and an ovarian graft made. The patient, who at the present time was aged about 40, had menstruated regularly for fifteen and a half years, but menstruation was now "slight"; she stated that she had had no pain nor a day's ill-health since her operation. Another patient had menstruated regularly for thirteen and a half years, after which there was a premature menopause at the age of 35½. Meanwhile she had been happily married. Again, a third patient was menstruating regularly when last seen, six years after operation. Unfortunately, the ultimate history of most of the patients had not been obtained. With the best intentions and the greatest care it was difficult to secure uniformly satisfactory—whether negative or positive—after-histories. Every operator should depute the analysis to some other person.

The question of the menopause itself was not always easy to determine, for some patients complained of hot flushes, headaches and the rest, even though they menstruated regularly. Leading questions should be avoided.

It was most important, also, in estimating the value of ovarian grafting in the absence of menstruation—which was usually impossible after hysterectomy, although two of his own patients on whom supravaginal hysterectomy and ovarian grafting had been performed, had menstruated subsequently—to be careful to exclude the initial menopausal symptoms following operation. For example, in Case 153, the patient was aged 34; supravaginal hysterectomy for fibromyomata uteri and bilateral salpingo-oöphorectomy with ovarian grafting had been performed. For six months there were menopausal flushes, which then ceased entirely, when evidently the graft functioned. This might be regarded as a successful case.

The use of grafts of the uterine mucosa along with ovarian grafts, as practised by Dr. Cheval when the uterus was removed, had interested him, the speaker, very much, for at one time he had himself believed that the ovaries would not remain functional after removal of the uterus and tubes. Indeed, Abel and Zweifel and Alban Doran had stated thirty years ago that the gonads atrophied after panhysterectomy. This, however, was not confirmed by experimental work at that time, but he (the President) had suggested in a letter to the *British Medical Journal* in 1906 that the failure to remove the tubes in the experiments might have accounted for the differences observed. In 1906 he had expressed the view that the uterus had an internal secretion which he called "uterin." However, he (the President) was now doubtful whether the uterus had a true internal secretion or whether the mucosa was essential to the integrity of an ovary with a normal blood-supply or of a well-vascularized graft. Further experimental work should settle the question. Nevertheless, as menstruation itself was of importance to the patient, when supravaginal hysterectomy was performed for fibromyoma in young women, some endometrium should be left.

In his own 218 cases he had, in addition to bilateral salpingo-oöphorectomy, performed acrohysterectomy (wedge-shaped fundal removal) in 122, low supravaginal hysterectomy in 27 and total hysterectomy in 18. In all cases of acrohysterectomy menstruation had been considered possible.

In this connexion it was interesting to note that in an analysis made in 1925 of his cases of acrohysterectomy to that date, in 68% of the cases with an ovarian graft the women were found to have menstruated subsequently, whereas 89% of the women in whom an ovary was preserved in situ had menstruated.

The procedure of ovarian grafting in the human subject could probably be further perfected. One adjuvant, which had suggested itself to him, as it had to Dr. Parkes, was the administration of prolan to stimulate the functions of the graft. Yet it should be remembered that at both the natural and the artificial menopause there was increased activity of the pars anterior of the pituitary with a large output and excretion of prolan (A), and this alone might be sufficient, and account for the readiness of grafted ovarian tissue to "take." The percentage of successes by the present method showed that the procedure was not only scientific and practicable, but also beneficial, when performed with skill and judgment.

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Dr. Cheval (in reply to Dr. Herbert Spencer) said that one of the advantages of the grafting of ovarian fragments in the superficial tissues was that if cystic or malignant change occurred, the change would be recognized early and access would be easy and free from danger. For the same reason infection of uterine grafts could only produce a superficial abscess. The danger, however, was largely theoretical: in practice he had not had to remove one of his uterine grafts on account of suppuration. He shared Dr. Spencer's hope that at some future date chemical science might provide a preparation which, when given by mouth, would prove a complete substitute for the secretions of the missing ovaries. Until that day arrived ovarian grafts were the best remedy.

Dame Louise McIlroy had suggested that there was a risk of malignant degeneration in the artificially formed endometriomata. He (Dr. Cheval) considered this risk illusory. There was no recorded instance of malignant change in accidental endometriomata in laparotomy scars.

He had been especially happy to hear Professor Blair-Bell, whose wide experience with ovarian grafts, extending over twenty years, gave unique value to his expressed views.

Section of Odontology

President—Sir NORMAN BENNETT, M.B., L.D.S.E.

[*February* 26, 1934]

Three Cases of Neuralgia.—ROBERT BRADLAW, L.R.C.P., M.R.C.S., L.D.S.E.

I.—Dorothy R., aged 28, a nurse, complained of pain in the left infra-orbital region, which was at first shooting in character but afterwards became a dull and constant ache (diagram 1). She had first noticed it six months ago, but during the last six weeks, when she was put on night duty which she disliked, it had become worse. She thought that the pain was more severe in cold weather and at the end of the day or if she was worried about her work or trying to concentrate on studying for her examination, in which she had previously failed. She had at that time three difficult nursing cases which gave her a good deal of anxiety. There was nothing

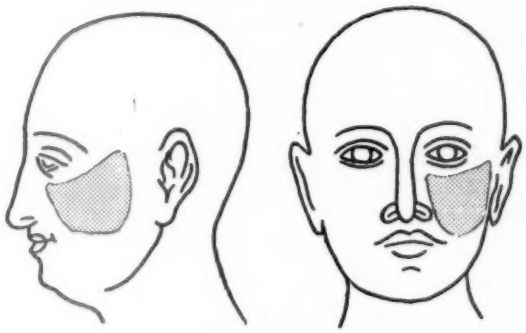


DIAGRAM 1.

relevant in the family medical history; her general health was good, and she had had no previous illnesses other than scarlet fever and measles when a child. She had had, however, some pains in her legs which her doctor thought might be rheumatic but which she herself thought were due to excessive standing. She slept well and her appetite was good. On examination marked tenderness to pressure was found over the left infra-orbital foramen and slight tenderness over the left mental foramen. All the teeth were present and neither the first inspection nor radiographs showed any abnormality. None of the teeth were tender to percussion or gave any unusual reaction to electrical or thermal stimulation. There were, however, three amalgam fillings in the left upper first and second molars. These fillings were removed and sedative dressings were substituted. As these afforded no relief, a

further examination was made when a small cervical cavity was found on the labial surface of the left upper canine, almost entirely hidden by the gum margin. The caries, although not extending laterally, had penetrated deeply into the dentine, and a temporary filling was inserted. The pain then became so much worse that it was thought expedient to extirpate the pulp. Persistence of the pain, although some-

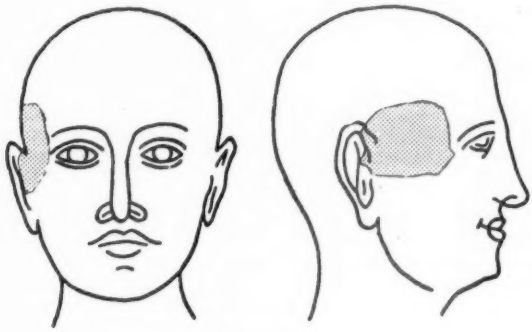


DIAGRAM 2.

what less severe in character, led to the patient insisting on the removal of the tooth. This was done and was followed by complete and lasting relief. A section was made, which showed that pulp tissue still remained in situ. This case emphasizes, first of all, the difficulty of completely removing the pulp in even a single-rooted tooth, and also the danger of failing to recognize organic lesions in a person of neurotic tendencies.

II.—Annie L., aged 60, complained of pain on the right side of the face which started suddenly about eight months ago. It persisted for three months, after which she had complete relief for four months. Then the pain recurred and lasted for another three or four months, after which there was a remission of two months. She had had her present attack for nearly three months, during which the pain increased in severity and affected a wider area. It began in the right temple and then spread to the forehead, above the eyebrow, and later involved the side of the nose, the orbit and the upper and lower lips (diagram 3). It was, however, entirely right-sided and had not affected the tongue. It was stabbing in character and the paroxysms lasted about five minutes ; during the pain the patient could not open her mouth to talk or eat. She thought that pressure on the right temple gave relief. Lachrymation, but no muscular spasm, accompanied the pain, which prevented sleep at night. The patient was not constipated and had always been healthy. She had no worries or anxieties. The nasal and frontal sinuses were reported free from disease. The face appeared to be normal. There was no loss of muscular tone but there was marked hyperæsthesia over the whole of the right side of the face and forehead and marked tenderness to pressure over the infra-orbital foramen.

In the mouth there were only four lower premolars and five upper molars present, the other teeth having been extracted many years previously. None of these teeth appeared abnormal on clinical examination but radiographs showed that pulp-stones were present in the right upper second and third molars, that there was interstitial caries on the distal aspect of the right upper second molar which also showed evidence of periapical infection. These teeth were extracted under nitrous-

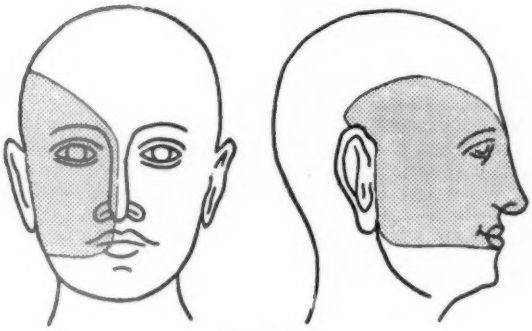
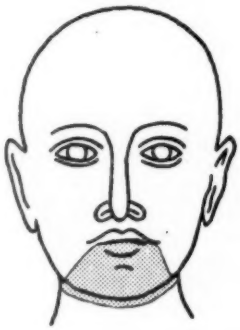


DIAGRAM 3.



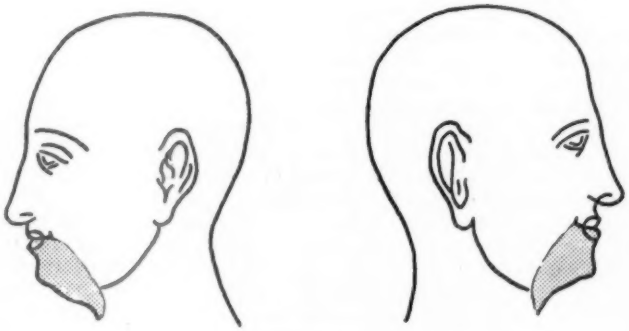


DIAGRAM 4.

oxide anæsthesia, and subsequently there was complete relief for eleven months, when unfortunatly the pain returned as severely as before. Several pulp-stones of varying size were found in both teeth. Some of these were not in relation to nerve-bundles, but in one case there was a calcific nodule actually laid down in the substance of a nerve-trunk and in another the pulp-stone could be seen to be diverting the nerve fibrils.

The interest of this case of paroxysmal trigeminal neuralgia lies in the fact that it illustrates what only too often occurs in reported cases of cure, in which, if they were subsequently followed up, a history of recurrence would be obtained.

III.—Lily I., aged 59, complained of a dull but persistent pain in the mental area and along the lower border of the mandible and neck. This she had had for some years, but until latterly when it had become worse she thought it was due to "the strain of her plate." She was a frail, emaciated old lady with a high colour and she had not been well for the past ten or twelve years. Two years previously she had consulted her doctor who found her to be suffering from diabetes. She had been unwilling to have insulin administered and had since then been on a very strict diet, from which almost all carbohydrate had been eliminated. She had in the past complained from time to time of pains and tingling in her limbs, which had previously been regarded as rheumatic, but which her doctor now thought were due to her hyperglycæmia. Her sight was bad; her appetite and digestion were good but she was constipated. The pain was more or less constant but was not sufficiently bad to keep her awake at nights, when it was certainly not any worse. Her temperature was subnormal and her pulse hard and rapid. She had marked arteriosclerosis and and her blood-pressure was 220 mm. The urine was pale and of low specific gravity and contained sugar and slight albumin.

There was marked tenderness to pressure over the mental foraminæ on both sides and hyperæsthesia over the whole of the painful area. The patient was edentulous, except for two lower canines which supported her lower denture. These were not carious but were slightly periostitic and were exposed at the neck owing to the recession of the gum and loss of supporting alveolus. They were not tender to percussion nor did they react to thermal or electrical stimuli. On radiographic examination there was no periapical disease, nor was any abnormality other than the loss of bone found clinically. Diagnostic mental and simple infiltration injections of novocain gave relief, so that after some hesitation it was decided to extract both teeth. This was done and the patient has had complete freedom from pain since. The teeth were decalcified and sectioned. The pulp chambers were considerably diminished in size owing to the deposition of secondary dentine pulp and the pulp itself showed marked signs of degeneration. The odontoblast layer was almost completely absent and the nerve-bundles had lost their myelin sheaths and showed all the signs of degeneration described by Euler and Meyer. In this case the conductivity of the nervous elements must have been very largely destroyed but as Feldman has pointed out, the disintegration products of the pulp are sufficient to cause apical irritation. It would be interesting to know whether this condition was entirely due to the denudation of the necks of the teeth or whether the nerves of the dental pulp are as much affected by disordered metabolic processes as those elsewhere in the body. It is of course possible that the hyperpiesis played some part in the production of pain. Rollinson, Whittaker, Kennedy and others have pointed out the very frequent association of arteriosclerosis with trigeminal neuralgia, and Praeger, Walkhoff, Fischer and Meyer have suggested that owing to the disposition of nerve-bundles in the pulp, compression by enlarged blood-vessels might readily occur and be productive of pain.

Oral Screens in the Treatment of Certain Dental Irregularities

By H. O. DICKIN, L.D.S.Eng.

MANY years ago I heard that it is possible to fit a shield within the oral vestibule for the prevention of mouth-breathing during sleep. The idea was fascinating; and the practical way to arrive at a suitable design seemed to be to make one, as an experiment, for myself. This screen turned out to be indispensable, and it still serves, despite the loss of most of the natural teeth in the meantime.

The method was adopted for many patients—some of whom were edentulous; and in the after-treatment of war-injury of the face. I know that such treatment would be a great boon to many of the edentulous, particularly for those in whom there has been extensive destruction of the tissues; such often suffer from laryngeal symptoms.

The screen-wearing adult finds the nasal air-ways becoming increasingly free as the years pass, which would appear to indicate some modification in the form of the soft tissues.

Throughout all this time I have not had the good fortune to meet any patient acquainted with this treatment, nor have I seen any screen made elsewhere.

It is difficult to understand why the oral screen is not better known; it has no rival for the relief of the infirmity of mouth-breathing during sleep. Surely this effective device must have been applied only to an infinitesimal proportion of those who would be likely to benefit.

The oral screen is a static device. Broadly speaking, all it does is to prevent mouth-breathing during sleep, and, by so doing brings into play a number of important natural forces.

When the lips are closed, or whilst a screen is worn, there is a negative air-pressure within the mouth; that is, a pressure below that of the atmosphere. The tongue is held back, so that its full bulk is available for spreading the dental arches, and for increasing the height of the bite, if all this happens at a period when any development of the framework of the face is possible. The mouth does not become dry. Within the nasal system there is an alternating positive and negative air-pressure, due to the pumping action of the lungs. The air passing through the nose is warmed, and thoroughly moistened.

If this perfectly normal function is present throughout the entire period of the growth of the framework of the face, it is probable that the whole face will exhibit harmony of size and form in its relation to the cranium, with larger dental arches and a flatter palate, when compared with the face of another more or less given to mouth-breathing during sleep.

The diagnosis of slight degrees of mouth-breathing during sleep may not be easy. Any such patient will be certain to deny it, if challenged directly. All these nocturnal mouth-breathers do not advertise the fact by snoring; nor do all the dry mouth; nor must we wait for a case until experience someone is found with "the vacant look," or some obvious sign of mental instability.

Where the least doubt exists, or if the teeth are found to be coated with film, or if dental caries tends to run riot, or if the gums show chronic superficial inflammation, a screen should be fitted. Where there is a history of common colds, tonsillar trouble, or, especially, some infection of the air-sinuses, there is so much the more reason for the use of a screen.

I hope to show that those natural forces, which can be brought to their proper function by this means, offer advantages over other methods in the treatment of certain dental irregularities; and that, additionally, some, or all, of the following benefits will be found to accrue: An increase in the strength of the lips; an expansion of the dental arches, and also of the true bone of the face; an increase

in the height of the bite; a reduction in the incidence of dental caries; a greater resistance to infections of the air-spaces of the head; an improved peripheral circulation of the blood throughout the whole body, being evident in the colour of the cheeks, and greater warmth in the extremities; a brightening of the mentality, due to the better aeration of the air-sinuses; more tranquil sleep; an increasing harmony of the features, not confined to the dental arches; a surprising improvement in the whole physique.

Full confidence in this treatment was only arrived at slowly. Recently I have found the models of a boy who was treated by this method for the reduction of slight maxillary protrusion sixteen years ago. It was not until several years later that other methods were abandoned. It did not occur to me that the subject might be demonstrated some day. Consequently, in the five cases now to be illustrated, the models available are merely those obtained to check progress at certain stages.

For the purpose of this present argument it is expedient to disregard all causes of dental irregularity other than those which may be associated with abnormality in breathing.

Case I.—A boy, aged 7 years 6 months, was seen in 1920. He suffered from severe asthma, and was unable to lead an ordinary life. The remaining carious deciduous teeth were removed. Maxillary protrusion was evident, yet any retractive device was contra-indicated by his poor health.

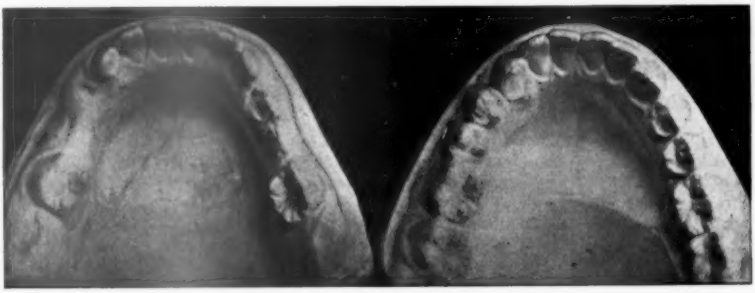
10 years 6 months. 13 years 3 months.

FIG. 1.—Case I.

10 years 6 months 13 years 3 months.

FIG. 2.—Case I.

A year later both maxillary first premolars were removed. In 1923, at the age of 10 years 6 months, I constructed a screen with a view to testing his tolerance to any form of appliance; my intention being to use an orthodox regulating device as soon as possible. He was not seen again for eight months, by which time a remarkable reduction of the



10 years 6 months. 13 years 3 months.

FIG. 3.—Case I.

protrusion had occurred and, which amounted to more in the circumstances, better health was reported.

During the next two years he was seen very occasionally. Then the second pair of models was prepared (figs. 1, 2 and 3). The asthma had gone, and the boy was at school. He then left the district, and has been lost sight of.

Attention is directed in this case, and in those to follow, to the increase taking place in the height of the bite, and also to the condition of the palatal tissue immediately behind the incisors in the later model shown on the right. I have not found this tissue to become thickened and inflamed in cases treated solely by screens. This point should be watched in the subsequent similar presentations of upper models.

During the progress of this case I became convinced that I must abandon other methods for the reduction of maxillary protrusion.

The word "mouth-breathing" has become time-honoured. The origin of much ill-health has been attributed to it, in some quarters, for many years.

I think that this word "mouth-breathing" has become a hindrance to the study of the infirmity; not "mouth-breathing," but "mouth-breathing during sleep" is the term which should be impressed upon students.

The following remarks are offered in support of the view that the real injury to health lies in the mouth-breathing which occurs during sleep.

In conversation with a friend, who has had a long experience of the treatment of dental irregularities, I mentioned my success in the reduction of maxillary protrusion by the prevention of mouth-breathing during sleep. He replied, "I can't see how you do it. Surely what you may gain during the night, you must lose in the day." What explanation is possible except that mouth-breathing may be disregarded during the day, so long as it does not happen during the night? If maxillary protrusion may be reduced, though treatment during the long hours of active life be utterly neglected, it is probable that all the far-reaching evils of the infirmity need no other treatment, so far as the correction of breathing is concerned. The whole of my experience supports this view.

In this connexion I will refer to the case of a woman, who had an old-established nasal trouble. Several times each year her sleep and health had been wrecked by the heavy discharge. It is twenty years since her last nasal operation and she had lost hope of improvement.

After a special screen had been in use for only five nights she told me of a great change for the better. She said, "I did not know that I was a mouth-breather until I used this screen. I feel that now I can breathe as well as I did just after my operation." And this in spite of the fact that for the last two of these five nights the screen had cut deeply into the tissues, having been accidently damaged whilst out of use. Even with this painful condition a struggle had been made to carry on, for the screen had been found to afford tranquil sleep. What radical cure of the mouth-breathing by day could have been accomplished by using a screen for a night or two?

Case II.—This girl was aged 8 years 2 months when the screen was fitted.

The maxillary first premolars were removed three months later, by which time the protrusion had almost disappeared. The models show the change in two years; at which time the mandibular first premolars were extracted.

There are no later models. Four years afterwards, that is at the age of 14, my notes state that there were no gaps remaining in the arches, and excellent dental articulation.

Case III.—This case, and the one following, show the rapid progress made in the first three and half months of screen treatment.

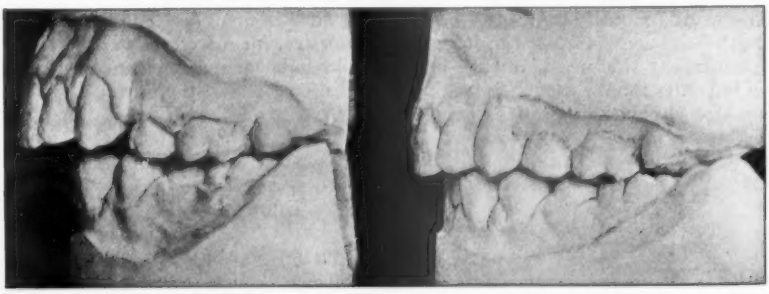
A girl, aged 9 years 3 months, had received orthodontic treatment. This patient had been sent to me by a friend, with absolute freedom as to future advice and treatment. After examination, I wrote to him saying that I preferred the screen method to the one in use, to which he most kindly agreed. A screen was fitted, and a month later both maxillary first premolars were removed.

I regard the forward inclination of the mandibular incisors as undesirable in this type of case. Therefore, the mandibular first premolars have since been removed. The case remains under treatment.

Case IV.—These are the models of the dental arches of the brother of the girl just mentioned. He reached me at the same time as his sister, and under similar circumstances, I was told that he had had lengthy orthodontic treatment.

I have removed no teeth whatever. At some previous time both maxillary first premolars, and also a lower incisor, had gone.

A screen was fitted at the age of 12 years 7 months, and the patient left for school.



12 years 7 months. 12 years 11 months.

FIG. 4.—Case IV.

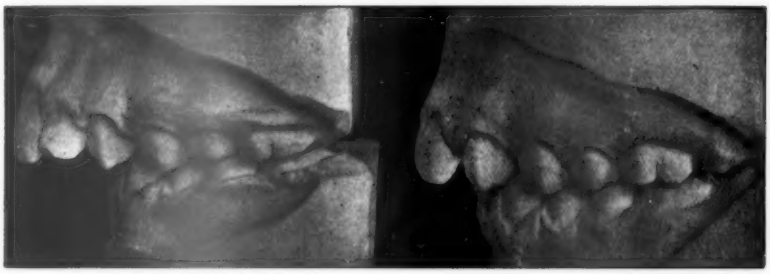
He received no intermediate attention. These models show the change in three and a half months (fig. 4). An improvement in health was reported. The outward movement of the second left premolar will be noticed. In passing, I wish to say that premolars generally have a way of clearing the cusps of their opponent teeth, under screen treatment, in a fashion which has taken me by surprise. I had anticipated having to trim the cusps in some of the cases undertaken, but not among those shown to-night.

The patient's mother has just expressed the opinion that the whole face of this boy has improved in harmony of the features, and not merely the arrangement of the teeth. The case is still under treatment.

Case V.—A screen was fitted for this girl at the age of 11 years 6 months. The maxillary second incisors were removed a few days later.

The forward movement of the mandibular incisors will be observed; and, once again, the increase in the height of the bite. This has occurred within twenty-six months (figs. 5 and 6).

Attention is directed to the importance of designing new screens as the position of the teeth changes.



11 years 6 months. 13 years 8 months.

FIG. 5.—Case V.

11 years 6 months. 13 years 8 months.

FIG. 6.—Case V.

One consideration is that the screen becomes too narrow in the premolar region as it travels backward. This may delay, or prevent, the natural expansion in the premolar region.

Screens are such comfortable and agreeable contrivances that they are apt to receive less attention than they deserve in these cases in which teeth are moving.

The case is still under treatment.

Consideration of these five cases must have made it clear that irreparable damage had been done to the growth of the framework of the face before treatment began. The truth is that much of the growth lost during early years cannot be regained by any treatment whatever.

I understand that measurements of skulls have shown that the normal breather

has about twice the cubic capacity in his maxillary sinuses when compared with those of a mouth-breather. Between these extremes must lie many intermediate degrees of loss of growth.

How can the permanent first molars be expected to occlude correctly when breathing has been abnormal throughout the development of the maxilla? The maxillary arch has failed to expand to its full possibility, and the mandibular molars may lean inward, possibly in the compensation of nature, and, principally, owing to the projection of the tongue during sleep, thus reducing its bulk in the molar region.

These five cases have been illustrated to substantiate my claim that the restoration of normal breathing during sleep is the best means available for: The reduction of maxillary protrusion; the projection of mandibular recession; the greatest legitimate expansion of the arches; the most orderly arrangement of the teeth within each arch; the most useful occlusion the circumstances will permit; the greatest increase in the height of the bite, of a permanent character, obtainable.

I will now refer briefly to three other forms of dental irregularity.

A case of open bite in a boy aged 8 years 6 months is at present under treatment. The arches are otherwise good; there is the usual history of what the textbooks call thumb-sucking.

No promise of success has been given; indeed the intractability of the deformity has been explained. During the first three months of treatment, whilst the boy has been away at school, the improvement in the appearance has been sufficiently marked to be gratifying to those concerned.

The term "thumb-sucking" seems an inaccurate description of what goes on in these cases. There is some nasal obstruction, possibly very trivial. The patient is almost a normal breather, with the natural tendency of the normal breather to keep the lips closed during sleep. The thumb is used merely as a prop between the teeth to maintain an air-way through the mouth. Once again it is obvious that the screen treatment should have been begun some years earlier.

I do not know how early in life such treatment may be practicable. For some children I think it might be begun at the age of 3 years.

One well-known danger signal should not be disregarded. If from the age of 4 years onwards, there is no adequate normal spacing to be seen about the deciduous incisors, it is high time that a screen should be brought into service; already much valuable growth of the framework of the whole face must have been lost. To permit this condition to pass untreated, as I must have done upon innumerable occasions, with some gloomy forecast of the probability of future dental irregularity, is certainly no longer to be justified in the light of my present knowledge.

Heredity of maxillary protrusion has not been found to increase the difficulty of treatment. In fact, it is far over-weighed by the advantage that subsequent patients have a pretty close acquaintance with the one undertaken first. I refer to instances in which the deformity is found in two generations, and in more than one branch of the same family. Should not this lack of difficulty on the score of heredity be borne in mind when occasion arises to attempt to treat the so-called mandibular protrusion? A convenient classical example was discussed briefly in *The Times* in July 1933, by Mr. W. Rushton and Professor William Wright, under the title of "The Hapsburg Lip." The waxen effigy in Westminster Abbey of the Stuart King Charles II had just been restored, and the photograph of the profile published (fig. 7).

One of the great-grandmothers of Charles II was a Hapsburg. The correspondence included the opinions: that the protrusion of the lower lip is secondary to that of the lower jaw; that the projection of the lower jaw may be relative rather than real; that the flatness of the infra-orbital region is the result of subnormal development; that this would be associated with a small maxillary antrum; and that the down-drag of the facial muscles accounts for the full eye (fig. 8). All these defects were attributed to mouth-breathing by Mr. Rushton.

It would be unfair to assume from this newspaper correspondence, which may have been abbreviated editorially, that all factors, other than mouth-breathing, had received no consideration. The contribution to this deformity attributable to other factors, if any, may be better estimated when a weight of evidence has become available showing the result of the prevention of mouth-breathing during sleep, from infancy, among those in whom there may be reason to anticipate such subnormal development of the maxilla.

This portrait of the Emperor Charles V is by Amberger (fig. 9). For my immediate purpose the truth of the draughtsmanship is fortunate. No attempt has been made to disguise the pallor of the face, or the deformity of the features. It is recorded that

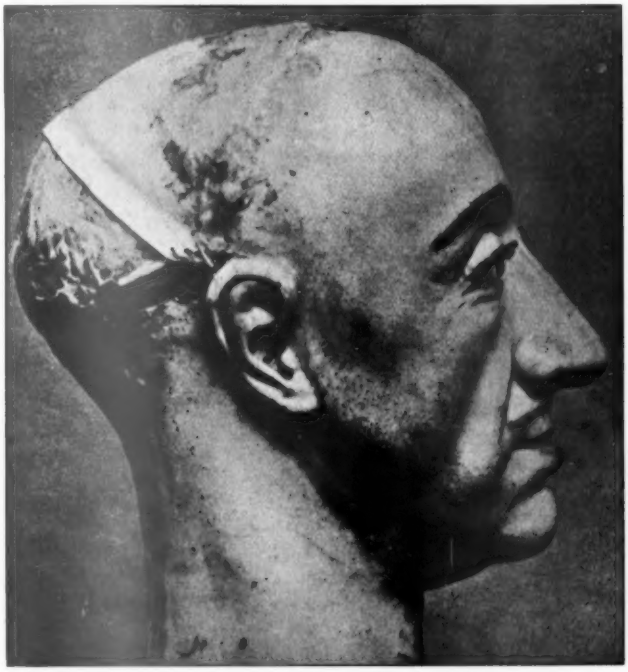


FIG. 7.—Charles II (Effigy).

Charles said that he knew that he was ugly, but that he did not think that he was so ugly as the painters made him appear.

Charles V was born in 1500, and died at the age of 58. Ill-health dogged him throughout life, and eventually compelled his retirement from the throne into private life. The illnesses, with which this able monarch was afflicted, have been attributed to over-indulgence in food. This looks as if some had been at their wits' end to find a vice of which to accuse him! We can be more sympathetic. It needs little imagination to picture the inefficient bite; the infection of the air-sinuses; the periodontal disease; the impaired peripheral circulation of the blood, evidenced

by the pallid countenance; the broken sleep; leading to chronic and painful indigestion. Doubtless food was taken frequently to attempt to allay the hyperacidity.

The last type of deformity, to be mentioned now, is the well-known close-bite. In close-bite the maxillary incisors may completely hide the mandibular incisors whilst the bite is in occlusion. The height of the mandibular molars above the floor of the mouth always appears to be much less than in the case of normal bite. I think that a part, at least, of this loss of height is to be found in the shallowness

FIG. 8.—Charles II (Honoré Pelle).

of the alveolar process of the mandible in the molar region, probably due to loss of growth in the ascending ramuses of the mandible. What is the cause of this loss of growth?

It may be thought that mouth-breathing during sleep can have nothing whatever to do with such a condition. Yet I know of adults with this defect who have used screens for many years, and to whom the screens are indispensable; these people must be definite mouth-breathers during sleep. I know also of children with this deformity who are not free from oral and pharyngeal infection.

Now it is known that the tongue is less bulky in the molar region during mouth-

breathing, and it has been shown, when dealing with maxillary protrusion, how the height of the bite becomes raised by the restoration of normal breathing during sleep. Are not these two points worthy of attention in the study of the ætiology of close-bite ?

Many observers have commented on the diminution in the size of the average modern face, when considered in its proportion to that of the cranium, if compared with the size of the average face in the portraits of our ancestors of the eighteenth century, and before. Examination of old skulls shows that lack of space for the third molars was not common.

FIG. 9.—The Emperor Charles V (Amberger).

An important factor operating to produce this diminution of the face is the increase of varying degrees of mouth-breathing during sleep, often considered negligible, from infancy onward. Extensive experience with screen treatment compels me to believe that a slight degree of mouth-breathing during sleep is not a negligible factor in the treatment of patients. Happily, it seems certain that the return to a more healthy and outdoor life, which has been one of the outstanding features of the present century, will lead in time to a decrease in the widespread

incidence of this disorder in breathing, the culmination of which has surely been reached among the less fortunate in the crowded cities.

A properly fitted screen produces no injury. None is shown radiographically, except that which is a legacy from the condition prior to the fitting of a screen.

Experience has shown that the more careful the watch maintained over the progress of a case, the better and more rapidly reached will be the desired conclusion.

For most cases a series of consecutive screens will be required to avoid the hampering of valuable natural growth. Each screen must be so designed that when it is in use the patient can forget it. Great care is needed to obtain the perfect start, after which the patient, however young, will be found a faithful guide to the comfort of future screens. Such comfort was well expressed the other day by the boy, whose models are seen in fig. 4. I had asked him if his screen remained comfortable. Smiling, he replied, "It is a part of myself."

JOINT DISCUSSION No. 6

Section of Neurology and Section for the Study of Disease in Children

[*March* 15, 1934]

Chairman—S. A. KINNIER WILSON, M.D. (President of the Section of Neurology)

DISCUSSION ON THE NERVOUS COMPLICATIONS OF THE ACUTE FEVERS AND EXANTHEMATA

Dr. J. D. Rolleston.—The present paper, which is mainly clinical in character, is based on observations in London fever hospitals during the last thirty-three years. I shall deal mainly with diphtheria and have only a few remarks to make on the nervous complications of the acute exanthemata and enteric fever.

Diphtheritic paralysis.—Frequency: Since diphtheritic paralysis first engaged attention, the records of its frequency have varied considerably with different observers. My own observations, based on a study of 2,300 cases of diphtheria, showed that 477 (20·7%) developed some form of paralysis. The much lower estimates made by other clinicians were probably due to several mild forms of palsy, such as a nasal voice or cycloplegia, having escaped attention. As I pointed out in my Oxford M.D. thesis nearly thirty years ago, to the majority of diphtheritic palsies the term paresis is more applicable than paralysis, so that unless a special examination is made in such cases, a slight and transient loss of power is very liable to escape notice. These semi-latent forms are well exemplified in the case of the two commonest palsies, viz., palatal paresis and ophthalmoplegia. In the mildest form the palatal affection is manifested by a slight nasal twang of the voice, while the impairment of movement of the palate on phonation is barely perceptible. The ocular palsy may be so slight that the pupils are of normal size and react to accommodation, although the patient may be more or less unable to read small print.

Age and paralysis: Contrary to the teaching of Landouzy, paralysis in my experience is more frequent in children than in adults, the great majority of cases occurring between 2 and 6 years of age. Not only actual paralysis, but abolition of the tendon-jerks is commoner in children than in adults.

Relation to character of initial attack: Several general physicians and neurologists whose experience of diphtheria in the acute stage is necessarily very small, have expressed the opinion that there is either no relation between the character of the faucial involvement and the frequency and severity of the subsequent paralysis, or that paralysis is actually more frequent and severe after mild than after severe attacks. Such a statement is in direct contradiction to the experience of those who have had prolonged and intimate acquaintance with diphtheria, such as the medical officers and nurses of large fever hospitals, who have always found that the frequency and severity of diphtheritic paralysis bear a direct relation to the character of the initial angina. The truth of this view can be confirmed by the practice—which I followed for many years—of classifying the case according to its severity, as soon as the throat became free from membrane. The incidence of paralysis among my cases

in which this plan was adopted was as follows: 48·1% among 800 severe cases, 13·6% among 498 moderate cases and 2·4% among 890 mild cases. Paralysis is much more frequent and severe in faucial cases in which the nostrils are involved than in purely faucial cases. Of 570 combined faucial and nasal cases, 240, or 42·1%, of which 133 were severe, developed paralysis, as compared with 237 paralysis cases (14·1%), of which 51 were severe, among 1,680 cases of faucial diphtheria, including laryngeal cases, but without nasal involvement. On the other hand, paralysis is extremely uncommon in purely nasal, laryngeal, or cutaneous cases without any faucial involvement, although undoubted examples of the kind have been recorded. Further proof of the direct relation between the character of the initial angina and the subsequent development of paralysis is furnished by the fact that among 40 relapses of diphtheria—occurring in hospital under my observation—in which the disease could at once be arrested by antitoxin, no instance of paralysis took place.

It is only when the faucial lesions have been overlooked or neglected and the case has been ambulatory throughout, or the recumbent position has not been enforced for a sufficiently long period, that severe and even fatal paralysis may follow mild angina.

Relation of paralysis to antitoxin: Closely connected with the question of the relation of paralysis to the character of the initial attack is that of the relation of the frequency and severity of paralysis to the day of disease on which antitoxin was given. I have frequently (1904, 1909, 1913, 1929) had occasion to show that whereas in pre-antitoxin times early treatment had no power to cut short the disease or prevent or modify paralysis, early injection of antitoxin undoubtedly jugulates the disease and tends to diminish the frequency and severity of subsequent paralysis.

Date of onset of palsies: During the first fortnight of the disease the only palsies likely to occur are palatal and cardiac paralyses. The term "precocious" has been applied to that form of paralysis of the palate which occurs in the first fortnight of the disease and is manifested by a nasal voice and, less frequently, by regurgitation of fluids through the nose. Like cardiac paralysis, it is almost invariably associated with malignant forms of diphtheria, as is shown by the high mortality, and the association of other grave symptoms during the acute stage, and subsequently by more frequent development of other varieties of paralysis in cases in which it occurs. According to Hochhaus, it is due to interstitial myositis of the palatal muscles. It is a grave sign, as it often precedes or accompanies a corresponding anatomical change in the cardiac muscle. Owing to its anatomical basis it is usually of much longer duration than palatal paresis of later onset. The term cardiac paralysis is usually applied to a syndrome arising after the membrane has disappeared from the throat, and consisting in alteration of the normal heart sounds, low blood-pressure, enlargement of the liver, oliguria—sometimes amounting to anuria—retching and vomiting. Death is preceded by an algid state, sometimes lasting for several days, during which no pulse can be felt. Milder forms of cardiac involvement in which complete recovery takes place are much more frequent. Contrary to what has been stated elsewhere, ocular palsy, in the form of cycloplegia, squint, or ptosis never occurs, in my experience, before the third week and rarely before the fourth or later. Cycloplegia usually precedes and is commoner than squint. Paralysis of the pharynx seldom occurs before the fifth week, when it is often accompanied by paralysis of the diaphragm, and, less frequently, of the abductors or adductors of the larynx. Between the fifth and seventh week involvement of the neck muscles, loss of power in the lower limbs and paresis of the facial muscles, especially of the depressor labii inferioris and platysma, are liable to occur. Sphincter trouble in the form of retention of urine and constipation or of incontinence of urine and fæces is also a later—but fortunately very unusual—occurrence. Sensory impairment, such as anæsthesia, hypæsthesia, astereognosis and pallanæsthesia—the detection of which in children is

often impossible—may occur at this time, usually in association with generalized paralysis.

Diphtheritic hemiplegia.—No account of diphtheritic paralysis is complete without mention of the rare form, hemiplegia, which differs from all other paralyses in diphtheria in being primarily a vascular lesion. Although several cases have been reported in various Sections of this Society in recent years, it is a very unusual event. Embolism, which is probably commoner in diphtheria than in any other infectious disease, appears to be the commonest cause, the cerebral embolism giving rise to hemiplegia being occasionally accompanied by renal or splenic infarction or other embolic processes. In all the cases on record the initial attack was severe. The onset of the hemiplegia is most frequent in the second or third week, when the heart is most severely affected. The prognosis is good as regards survival, but unfavourable as regards complete recovery of function, as contractures and atrophy usually supervene in the paralysed limbs, and as a rule there is some mental impairment. I have, however, seen and reported before the Section for the Study of Disease in Children (1915-16), two cases of diphtheria in which the hemiplegia, though complete and accompanied by the characteristic changes in the reflexes, disappeared within twenty-four hours, and I found references to four other examples in the literature. Although one patient recovered and an autopsy could not be obtained in the other case, the paralysis was probably due to uræmia in the former case and to microscopical embolism in the latter.

Encephalitis, giving rise to double hemiplegia or ataxia—of which cases were shown at a meeting of the Section for the Study of Disease in Children in 1931 by Worster-Drought and Hill—is a very rare occurrence. The same is to be said of chorea, of which Critchley has reported an example.

Reflexes: The tendon reflexes are affected in a considerable proportion of all cases of diphtheria, the knee-jerks in my experience (1905) being rendered sluggish or abolished more frequently than the ankle-jerks. In a series of 100 cases of diphtheria I found that the knee-jerks were lost in 31 and sluggish only in 38, whereas the ankle-jerks were affected in 47 cases only, being lost in 20 and sluggish in 27. Affection of the ankle-jerks was never found without a corresponding or relatively greater impairment of the knee-jerks. It is important to note that in only a small proportion of cases are the tendon-jerks lost in the first week of the disease, so that it is unwise to exclude diphtheria merely because the knee-jerks are active in a doubtful case of sore throat. It is important to realize that loss of the tendon-jerks may persist for many weeks after clinical recovery, so that their absence should not contra-indicate a patient's discharge from hospital. The superficial reflexes—notably the abdominal reflex in both sexes and the cremasteric reflex in the male—are lost only in severe cases of generalized paralysis, and such loss is usually only of short duration. Many years ago (1910), stimulated by a paper by Kiroff who had found Babinski's sign present in diphtheria, I examined the plantar reflex in 877 cases of diphtheria and found an extensor response in 172 (19·6%). Babinski's sign was found to be essentially a phenomenon of the acute stage, being replaced, in the great majority, by a flexor response in convalescence. It was not associated with any special condition of the tendon-jerks and was never accompanied by ankle clonus. It was more frequent and persistent in severe attacks of diphtheria than in mild attacks, and was most probably due to a transitory perturbation of the pyramidal tract by the circulating toxins, comparable to the slight degree of meningeal reaction which frequently occurs in acute infections.

Prognosis: Complete recovery in diphtheritic paralysis is the rule, death the exception. Apart from hemiplegia, which seldom ends in complete recovery, the rarest contingency is for the paralysis to become chronic. In view of the fact that I have not met with a single case during my thirty-three years' experience and that only eight have been recorded in the literature, the last of the kind having been

reported in 1906 (*Rev. Neur. and Psych.*, 1907, v., 56), I am inclined to think that some other cause than diphtheria must have been responsible for the chronicity. The prognosis usually depends on the age of the patient, the situation of the paralysis, and the date of onset. The older the patient, the better the prognosis, death from diphtheritic paralysis in an adult being, fortunately, a rare event. The onset of cardiac paralysis before the third week is of very unfavourable omen, whereas the later development of cardiac involvement is much less serious.

Precocious palatal palsy, as already indicated, is a grave sign, as is also the loss of the abdominal reflex in late generalized paralysis.

Treatment: Prophylactic measures in the form of early injection of antitoxin and rest in bed for a period varying with the severity of the initial attack are likely to be more effective than curative treatment. In the most frequent palsies, viz. palatal and ciliary, their transient duration and mild character render any special treatment unnecessary. The treatment of cardiac and pharyngeal paralysis is too well known to need discussion at a meeting of this kind. I have had no experience of the Drinker or other apparatus for artificial respiration in the treatment of diaphragmatic paralysis. Several French clinicians have strongly recommended the use of antitoxin in diphtheritic paralysis, but the natural tendency to spontaneous recovery and the failure of this treatment in experimental diphtheritic paralysis, as shown many years ago by Rosenau and Anderson and recently by Uhry, indicate that the success of the method is due less to a specific action than to psychotherapy.

Scarlet fever.—The nervous complications of scarlet fever consist in serous meningitis, which is not uncommon in severe attacks, suppurative meningitis which is usually secondary to otitis media, less frequently to rhinitis, and rarest of all primary, cerebral or cerebellar abscess which is usually otogenic also, and hemiplegia, of which I collected 75 cases in a paper read before the Section for the Study of Disease in Children in 1927. Peripheral palsies in scarlet fever, of which there are a few cases on record, are extremely rare and none have come under my observation.

Measles.—Although a good deal of attention has recently been given to encephalitis as a complication of measles, nervous complications of any kind are in my experience excessively rare in this disease. Meningitis, which is an infrequent occurrence, is usually otogenic as in scarlet fever, but in rare cases it may be primary. A few examples of myelitis, disseminated sclerosis, chorea and various psychoses have been recorded, but I have not seen any myself.

Rubella.—Nervous complications are very rare in this trivial disorder, and none have come under my notice, but examples of peripheral neuritis, Landry's paralysis, meningitis and encephalitis have been recorded, as I have indicated elsewhere (1929).

Varicella.—As in measles and rubella, nervous complications are uncommon in this disease. Although in recent years numerous examples have been recorded, especially of encephalitis, in the great majority of cases of this complication complete recovery is the result and death is very rare. Other nervous sequelæ of varicella are meningitis, myelitis and neuritis. An excellent survey of this subject will be found in the recent paper by Corda of Cagliari.

Smallpox.—The rarity of nervous complications in smallpox is shown by the fact that I could find only 25 examples among the records of 10,000 patients in the last great London epidemic which took place in 1901-02. Thirty years later Marsden and Hurst reported 11 cases of acute nervous symptoms associated with smallpox in patients aged from 6 to 46 years. Seven of these, of whom four recovered and three died, were examples of acute disseminated encephalomyelitis. Necropsies on the fatal cases showed lesions which were indistinguishable from those of postvaccinial encephalitis. Other nervous complications occasionally met with in smallpox are meningitis—which is most likely to occur during the stage of suppuration or desiccation—myelitis and peripheral neuritis.

Enteric fever.—In my experience nervous complications in enteric fever are rare, apart from abolition or impairment of the abdominal reflexes and delirium, which, as I pointed out in 1906, are rather symptoms than complications of the acute stage. With the exception of the condition of tender toes, I do not recall having seen a case of peripheral neuritis in typhoid fever, although this disease is reputed to come next to diphtheria in its tendency to attack the peripheral nerves. There is little doubt that some at least of the cases of peripheral neuritis occurring in typhoid fever are really examples of alcoholic neuritis of therapeutic origin. Meningitis may occur as an initial symptom in the form of meningo-typhoid or meningo-paratyphoid, or at a later period, and most frequently between the fifteenth and twentieth days. Recovery usually takes place in serous meningitis, while in suppurative meningitis death is the rule. Spinal complications consist in Landry's paralysis, transverse myelitis or a *forme fruste* manifested only by exaggeration of the reflexes, Babinski's sign and ankle clonus. Typhoid spine, which may occur in all but the mildest cases, usually arises in convalescence and consists in a spondylitis and perispondylitis. The symptoms are intermittent temperature, pain and rigidity in the dorsolumbar region and occasionally pain radiating to the abdomen and lower limbs. Cerebral involvement may be manifested by hemiplegia with or without aphasia. Psychoses may occur during the prodromal period, in the form of mental excitement or depression—during the height of the disease in the form of delirium or stupor, or during convalescence, in the form of acute delirium, confusional insanity, delusions, mania or melancholia.

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Dr. W. G. Wyllie.—A division of the nervous complications of the acute fevers and exanthemata into suppurative and non-suppurative types places the bulk of our material in the second group. In the first, or suppurative, type an invasion of the central nervous system by visible bacteria produces meningitis or cerebral abscess. Such events may occur in scarlet fever and typhoid, but are best known in connexion with pneumonia.

Any attempt to classify the non-suppurative encephalopathies must be made on a pathological basis, as the clinical syndromes are for the most part the common property of all the acute fevers. I propose, therefore, to use the following classifications: (*A*) The encephalopathies characterized by demyelination; (*B*) the toxic encephalopathies; and (*C*) the encephalopathies of vascular origin, hæmorrhagic, embolic, or thrombotic. Anatomically, the nervous complications of some of the acute fevers are represented in more than one of these groups.

Clinically, the commonest neurological syndromes following the acute fevers are: (1) A multiple focal or disseminated type with cerebral and spinal symptoms; (2) a mainly spinal type; (3) a cerebellar or ataxic form; and (4) a focal hemiplegic type. Any of these syndomes may be associated with each member of the group of fevers of virus causation—measles, smallpox, varicella and German measles. The most frequent central nervous complication of scarlet fever, whooping-cough, and

diphtheria is the focal cerebral hemiplegic syndrome. A purely meningeal syndrome—meningismus, serous meningitis—occurs as a complication of any of the acute fevers.

(*A*) *The demyelinating encephalopathies.*—The nervous complications of measles, smallpox, chickenpox, and German measles, have a strong family likeness, noticeable not only in their clinical manifestations but also in their morbid anatomy. Histological reports on cases following German measles are extremely rare, but in Bénard's [1] case of meningomyelitis there was the same demyelinating feature common to the other members of the group.

A striking feature of this group is the uniformity of the time-interval separating the appearance of the primary exanthem and the onset of the nervous symptoms—on an average, seven days. After smallpox it is commonly from five to thirteen days, after measles usually seven days, after chickenpox from seven to ten days. In post-vaccinal cases the average incubation period is the same. A shorter period, from three to seven days, is usual in the cases following German measles.

In this period of decline of the primary exanthem, when the patient is on the way to recovery and has become afebrile, the onset of the nervous symptoms is abrupt with a renewal of pyrexia. Symptoms of "meningism" or "serous meningitis" are common, headache, vomiting, cervical rigidity, Kernig's sign, and sometimes convulsions. Drowsiness is a prominent symptom and often deepens to coma lasting for several days. On the return of consciousness, the character of the nervous lesions becomes apparent, the cerebral including hemiplegia, diplegia and aphasia: the basal ganglia, choreiform movements; the brain-stem, rigidity, tremor, difficulty in speech or in swallowing; the cerebellum, ataxy; and spinal symptoms, paraplegia, sensory disturbances, and retention of urine. Trismus has been observed most often in cases following smallpox, vaccination, and chickenpox, but also after measles and German measles. Ocular palsies and nystagmus are infrequent, but papillœdema is present in many cases.

After measles, smallpox (and vaccination), combined cerebral and spinal, or mainly spinal, symptoms are most common. After chickenpox ataxy is the most frequent symptom, less often spinal symptoms. In the much rarer cases following German measles, cerebral, cerebellar, or spinal syndromes have been recorded.

The cerebrospinal fluid in all these cases gives very similar results. It may be normal, but is often under pressure, and shows a moderate pleocytosis, or sometimes as many as from two to four hundred cells, mainly lymphocytes. More rarely a turbid fluid is encountered, especially after measles, with a preponderance of polymorphonuclear cells.

The rate of mortality in the cases after these fevers is unequal. Following measles, Ford [2] estimates the mortality at 10%, but in the non-fatal cases the percentage with some residual incapacity, 65%, is much greater than after the other fevers in this group. In post-varicellar cases the death-rate is about 6%. Three deaths occurred in Marsden and Hurst's [3] ten cases following smallpox. In post-vaccinal cases the average mortality is from 30 to 40%.

What has been the relative frequency of the nervous complications of these fevers? Those following measles, smallpox and vaccination have been recognized for over a century, but mostly as isolated and widely spaced instances. Still fewer records are available of cases following chickenpox and German measles. The striking feature of the cases following measles, chickenpox, smallpox and vaccination, has been their increased prevalence in recent years. Between January 1893 and December 1927, in a series of 15,000 cases of smallpox in the Metropolitan area, Marsden and Hurst found the record of one case only of an ascending myelitic type, but between 1928 and 1931, out of 40,313 cases of smallpox notified in England and Wales, there were nine cases with nervous complications. The increased number of cases following vaccination since the year 1922 is well known. In measles

especially the figures have gone up since 1924. In England for the four years, 1927 to 1930, of fatal cases alone there were 25. For post-varicellar cases, Dagnelie, van Bogaert [4] and others estimated from the literature a total of 69 cases, of which 50 occurred since 1920, with 13 cases in the year 1930 alone.

The family likeness, therefore, in this group is shown by: (1) a similarity of symptomatology; (2) a remarkable uniformity of the incubation period; (3) an independence of the nervous complications in regard to the severity of the primary exanthem, or to the size of the epidemic; (4) an increased incidence of the post-infectious demyelinating encephalopathies within the last twelve years; and (5) a co-existent increase of spontaneous cases, clinically and anatomically similar—acute spontaneous encephalomyelitis.

(*B*) *The toxic encephalopathies.*—In this group the toxins of specific bacteria are the agents whereby the nervous complications are produced. Toxic degenerative changes are met with, especially in whooping-cough and scarlet fever, but may also occur in many other acute infections, pneumonia, erysipelas (Eckel [5]), streptococcal, pharyngeal and otitic inflammations. The symptoms are those of meningism, serous meningitis, or a meningo-encephalitis. Some of the cases of post-scarlatinal hemiplegia are of this nature. The nervous symptoms may arise at any time, either early in the fever or not until later, in the period of desquamation. In whooping-cough the onset of the nervous symptoms is often delayed until after the period of paroxysmal coughing has practically ceased. Then there occur multiple convulsions, or whooping-cough eclampsia, in some cases accompanied by hemiplegia, diplegia, idiocy, and blindness (Baginsky [6], Schmitt [7], Turnowsky [8]). Most cases of pertussis eclampsia are fatal. Visual disturbances, amaurosis, are more common in whooping-cough than in scarlet fever. In the former they may be due to hæmorrhage, encephalitis, papillitis and thrombosis of the central retinal artery (Weigelin [9]). As an example of a meningo-encephalitis complicating a throat and ear infection, I saw recently a boy, aged 6 years, who, four days after the commencement of a moderately severe pharyngitis and otitis media, suddenly developed continuous left-sided fits, coma, hemiparesis, with bilateral extensor plantar responses, knee- and ankle-jerks abolished, a transient inequality of the pupils and facial hemiparesis. The cerebrospinal fluid was clear and contained 50 cells, mainly lymphocytes. He recovered completely.

The pathology in this group of neuropathies has been described in some cases as acute hæmorrhagic, and in others as acute toxic, encephalitis. The effects of the bacterial toxins are seen most conspicuously in the cortical ganglion cells and in the small blood-vessels. In post-pertussis cases there is extensive ganglion cell-degeneration (Husler and Spatz [10]). Grinker and Stone [11] have emphasized the frequency with which a capillary endothelial proliferation is found in the toxic encephalopathies following some of the acute fevers and other acute infections, and also in apparently spontaneous cases, possibly due to endogenous toxins. A similar feature has been observed in cases of food poisoning, and can be produced experimentally with inorganic poisons.

Acute toxic encephalitis has also been recorded after measles, smallpox, and mumps. Such cases following measles have no typical incubation period, as the nervous symptoms come on early or late and have a closer relation to the severity of the toxæmia of the primary fever than in the demyelinating group. Similarly, in smallpox, Marsden and Hurst describe a case of acute toxic encephalitis with symptoms commencing three days before the appearance of the rash.

An unusual syndrome, probably of toxic origin, is obesity. I have notes of five cases, three of which were given to me by Dr. R. W. B. Ellis. There were three cases as a complication of scarlet fever, one pneumonia, and one mumps. Polyuria was absent, and in the two male children no evidence of genital regression was observed. In both my cases the severity of the primary illness, scarlet fever and

pneumonia, was so extreme that the child's life was stated to have been despaired of. I am inclined to place the lesion not in the pituitary, but in the region of the floor of the third ventricle.

The cerebrospinal fluid in the group of toxic encephalopathies is usually normal, but may contain a moderate increase of lymphocytes up to fifty cells or so, and a slightly raised protein percentage.

Toxic encephalopathies, due to the diphtheria toxin affecting higher neurones, are very rare. A case of this nature, presenting choreiform movements has been recorded by Critchley [12].

(*C*) *Encephalopathies of vascular origin.*— Hæmorrhage, embolism, and thrombosis as a cause of hemiplegia in scarlet fever and whooping-cough, have acquired in the past an importance based on very insecure evidence, as many of the cases reported have been made without anatomical verification. In scarlet fever the primary cause of the hæmorrhage may be uræmic. Goodall [13] records a case of subdural hæmorrhage in a boy aged 9, coming on thirty-three days after the commencement of a mild attack of scarlet fever.

In whooping-cough, especially in the early stage of the disease, cerebral thrombosis may occur as a result of asphyxia during a severe bout of coughing. The hemiplegia may be temporary or permanent, depending on the severity of the vascular lesion. In diphtheria the onset of hemiplegia is usually in the second or third weeks, according to Rolleston, and the vascular lesion is commonly embolic from a ventricular endocarditis.

(*D*) *Mumps meningo-encephalitis.*—There is apparently a direct connexion between the virus of mumps and its nervous complications. The virus is recognized to possess potential neurotropic properties. Even in the absence of nervous symptoms, a pleocytosis, mainly lymphocytic, has been noted in the spinal fluid in many cases. Symptoms of meningitis, less often meningo-encephalitis, may precede the glandular tumefaction (Weissenbach [14], Rompe [15]), but more commonly occur during the first eight days following the parotitis—sometimes as late as a month afterwards. More rarely, a polyneuritic syndrome has been observed, with flaccid paralysis of all four limbs, and sometimes ocular nerve palsies, facial paralysis, and deafness. The nervous symptoms may persist for several weeks, but in most cases recovery is complete.

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Dr. J. G. Greenfield: The scope of this discussion is so vast that I propose to touch only on the pathological aspect of a few of the nervous complications of the acute specific fevers. Certain of these complications, viz. the neuritis of diphtheria, the meningitis or meningo-encephalitis of mumps and the encephalitis of typhus fever, are the direct effects on the nervous system of the ætiological agent. Other complications are common to several diseases. Such is the pathological condition which has been called acute disseminated encephalomyelitis (Westphal) or acute

perivascular myelinoclasis (Marsden and Weston Hurst), and such less-defined conditions as acute toxic encephalopathy, and hæmorrhagic encephalitis. In certain of the fevers, especially measles, these three complications or any two of them may be combined. Again, the nervous symptoms may be caused by arterial embolism, sinus thrombosis, or the invasion of the brain or meninges by pathogenic micrococci, or they may form part of the anaphylactic response to treatment by antitoxin.

It is unnecessary to add anything to this discussion about the first three complications, as they form part of the picture of the fully developed disease. With regard to *acute perivascular myelinoclasis*, we now have evidence that it may follow not only smallpox and measles, but also influenza, chickenpox and German measles. True the number of proved cases following each of the last three fevers is small, but fatal cases following influenza have been fully reported by myself and by Grinker, following chickenpox by Zimmermann and Yannet and by van Bogaert, and following German measles by Bénard. The last was a case of myelitis with the typical lesions. The chickenpox cases were not so typical. Zimmermann and Yannet found mainly toxic changes in the nerve-cells and small blood-vessels, although they thought there was also some loss of myelin round subcortical vessels. The case of Dagnelie and Dubois was similar, and the case reported by van Bogaert ran a prolonged course of seventeen days, and showed unusually severe and widespread lesions in the cerebellum as well as in the cerebrum. Still these cases afford some justification for attributing the nervous complications of these fevers to acute perivascular myelinoclasis. This name seems preferable to the old-established one of "acute disseminated encephalomyelitis," partly since the latter has been used, especially in Germany, for the more acute forms of disseminated sclerosis, but chiefly because the new name is merely a description of the pathological condition, and so avoids the temptation, to which our Chairman has drawn attention, of taking an uncommon pathological picture and calling it a disease. Such cases may have the clinical appearance of meningitis, and many have been reported under this heading. The examination of the cerebrospinal fluid, although valuable, does not always lead us to the correct diagnosis, especially when it contains one or two hundred cells per cubic millimetre, and although its other characters may convince the pathologist that the condition is not one of meningitis, he may fail to transmit his conviction to the clinician in charge of the case. As to the relationship of this condition to the diseases which precede it, we know no more than did Westphal and Barlow who first described it. All attempts to reproduce it in animals have failed, although something very like it has been found occurring spontaneously in monkeys.

Whooping-cough.—The nervous complications of whooping-cough have been well known and studied for many years, and the pathological changes underlying them are now well established. Neurath in 1904 was among the first to show that hæmorrhage plays a quite unimportant part in the picture, although the intense congestion of the tissues in patients dying in convulsions may lead to perivascular or subpial hæmorrhages as an agonal or post-mortem phenomenon. Dubois, Ley and Dagnelie have recently reported eight cases in none of which was cerebral hæmorrhage found. The changes consist, in the early stages, of small-celled infiltration of the meninges, and sometimes also of the more superficial cerebral vessels, with some œdema and congestion both of meninges and cerebral tissue. In addition there are toxic or degenerative changes in the pyramidal cells of the cortex and of the cornu Ammonis and in the Purkinje cells of the cerebellum. These often go on to death and disappearance of these cells, so that in some cortical areas only the granular cells are preserved. The neuroglial proliferation which has been described in the cortex is probably secondary to the loss of nerve-cells. Dr. Ellison has recently reviewed this subject so competently that little remains to be said on it. The theory, which he favours, according to which the changes in the nerve-cells are ischæmic and caused by temporary spasm of small vessels, is looked at rather

askance by physiologists, although it has the blessing of such masters of neuropathology as Spielmeyer and David Orr. In whooping-cough the association of these cell changes with meningeal infiltration suggests rather a toxic or infective causation. Fonteigne and Dagnelie have produced a rapidly fatal meningoencephalitis in guinea-pigs by the intracerebral injection of minute doses of a culture of the Bordet-Gengou bacillus, or by intracerebral or intracisternal injection of 1/40 to 1/50 c.c. of its endotoxin. These experiments show, at least, that the Bordet-Gengou bacillus has some affinity for the nervous tissues and they should be borne in mind in discussing the pathogenesis of whooping-cough eclampsia.

Meningism.—Meningism is a clinical term, and its pathological basis may vary. But all are agreed that it is associated with an increase of intracranial pressure. Whether this of itself produces the meningeal symptoms, or whether there is some other factor underlying these is undecided. What seems clear is that reduction of the cerebrospinal fluid pressure by lumbar puncture usually cures the symptoms. An interesting theory which accounts for this sudden increase of intracranial pressure has been recently put forward by Howe and Fremont-Smith. According to this theory, swelling of the brain and increase in quantity of cerebrospinal fluid are caused by the sudden lowering of the blood chlorides, or hydræmia, which takes place at the onset of many fevers. This causation was adumbrated by Mestrezat who found a greater reduction in cerebrospinal fluid chlorides in cases of pneumonia with meningeal symptoms than in those without, although the fall was not so great as in cases of pneumococcal meningitis. It is well known, since the work of Weed, that the intravenous injection of distilled water causes a sudden rise of intracranial tension, and a sudden hydræmia of the blood from any cause would be likely to have the same effect. Fremont-Smith has shown that even in fever induced by the intravenous injection of typhoid vaccine, as well as in malaria and rat-bite fever, hydræmia occurs during the rise of temperature, and is followed after a short interval by a fall in the percentage of chlorides in the cerebrospinal fluid. If meningism is caused by this hydræmia it probably depends on the rapidity with which dilution of blood takes place, and perhaps on other factors, among which idiosyncrasy may play a part. In Levinson's cases, for example, it was four times more common in boys than in girls. Although this author discusses the chloride theory, he adduces no definite evidence either for or against it, but his 50 cases show an average reduction in the cerebrospinal fluid chlorides to the neighbourhood of 660 mgm. His figures, however, do not distinguish the meningism of early pneumonia from that occurring with otitis media, in which the pathogenesis may be quite different. In individual cases of meningism, figures for cerebrospinal fluid chlorides as low as 600 mgm. are not uncommon. But even if they are found not to be greatly reduced, this does not invalidate the theory, since the initial hydræmia may be rapidly compensated and there is always a lag in the fall of cerebrospinal chlorides. Thus Fremont-Smith in a very large series of normal cases found the cerebrospinal fluid chlorides to have a fairly constant ratio of 120 or 125% to the blood-chlorides, but when the latter fell to very low levels as in tuberculous and pneumococcal meningitis the cerebrospinal fluid chlorides did not always fall proportionately and so the ratio might rise to 140 or 150%, or even, exceptionally, to 170%. This theory would also explain the occurrence of meningism as an occasional sequel to acute gastro-enteritis without fever, as in this condition there is a great loss of chlorides from the stomach and bowel.

Another cause for meningism is anaphylaxis. This is a comparatively rare phenomenon, but well authenticated cases are on record. In such cases there is a slight excess of cells, often with a few polymorphonuclears, in the cerebrospinal fluid. The best-known example of this is the meningeal serum reaction which occurs from the seventh to the tenth day in treated cases of meningococcal meningitis. But cases have also been reported after intravenous and subcutaneous injections of different kinds of serum.

The work of de Lavergne and Abel indicates that the meninges commonly participate to a slight degree in serum sickness, but grave complications of this kind are fortunately rare. Symptoms suggesting cerebral tumour with choked discs may occur and cases of this kind have been reported in which there was no skin rash. Apparently the commonest form of involvement of the nervous system in serum sickness is a palsy of the muscles supplied by one or both brachial plexuses, with pain but little anæsthesia (Allen). One may conjecture that this localization is determined by absorption of serum along the lymphatics of the nerves from the site of injection.

Finally I should like to consider briefly the subject of *sinus thrombosis*. The effects of this may be very great or very slight, according to the extent of the sinuses involved and the degree of anastomosis between the surface veins. If the latter is free, thrombosis of the superior longitudinal sinus alone does little more than divert the blood into other sinuses. There are usually at least three large anastomotic veins which drain the convexity of the hemisphere:

(1) The vein of Trolard, joining one of the anterior group of superior cerebral veins to the middle cerebral vein which drains into the cavernous sinus.

(2) One or two anastomotic veins of Labbé, which connect the middle cerebral vein with the lateral sinus, passing over the outer margin of the temporal lobe. These may also connect with the posterior group of superior cerebral veins.

(3) The basilar vein of Rosenthal running from the anterior perforated spot round the midbrain to the great vein of Galen provides anastomotic drainage from the mesial surface of the brain.

In many cases in which symptoms result from thrombosis of the sagittal or other sinus, we may see little macroscopic abnormality in the cortex. But here and there in microscopic sections we find areas from which all the nerve-cells have disappeared or in which they are shrunken and hyperchromic. The neuroglia and the other supporting structures usually remain intact. These areas are flanked by rather less affected zones which shade off fairly rapidly into healthy cortex. Such areas are most often found near the point where the large veins run into the thrombosed sinus and may therefore affect chiefly that part of the motor cortex which innervates the legs. Incidentally, the old theory which attributes diplegia to thrombosis of the superior longitudinal sinus cannot be discarded on the grounds that no such thrombosis can be found when the child dies months or years later. The clot may be absorbed and disappear but the destruction of nerve-cells is irremediable.

The effects of thrombosis of one lateral sinus chiefly depend on the freedom of anastomosis at the torcular Herophili. Although this sinus is most commonly affected in middle-ear disease it may become thrombosed in fevers and marantic states. We have in the museum at the National Hospital, Queen Square, the brain of a child in whom thrombosis of the left lateral sinus developed as a sequel to a severe and prolonged bout of vomiting. Unfortunately there was no anastomosis at the torcular Herophili, and the thrombosis spread to the great vein of Galen, causing intense hæmorrhagic infarction of the whole of the basal ganglia.

At the present moment there is some controversy as to whether thrombosis of the straight sinus or the great vein of Galen can cause hydrocephalus. I have evidence from one case that thrombosis of that lateral sinus which drains the straight sinus (usually the left) may, in the absence of anastomosis at the torcular Herophili, cause some degree of hydrocephalus. Stopford has indicated how partial obstruction of the straight sinus might play a part in increasing intracranial pressure by promoting the secretion of cerebrospinal fluid, but it is only fair to say that no valid experimental evidence has been brought forward to prove this relationship. Complete obstruction of the straight sinus or the great vein of Galen is likely to cause severe infarction of the region which it drains, and thus to destroy the choroid plexus rather than to increase the formation of cerebro-spinal fluid.

I have attempted in this review to focus attention on those parts of the subject

about which opinion is not yet fixed, in the hope of stimulating thought and discussion. I should like, finally, to enter a plea for the thorough examination of the brains—including the venous sinuses—in children who die of these complications. Unfortunately the brain is a large organ and when it is macroscopically normal we may easily fail to find the area of greatest damage; but a careful examination will usually reveal at least the type of lesion which causes the symptoms, even if its apparent extent fails to explain their severity.

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Dr. W. Gunn: The relation of acute encephalitis to the specific infectious diseases has perhaps received more prominence than the number of recorded cases would warrant and has diverted the attention of clinicians from certain other much less rare nervous complications or sequelæ, some of which are probably more amenable to treatment.

There has lately been a tendency to ascribe to encephalitis a variety of mild meningeal and cerebral disturbances; as recovery is the rule the exact pathological condition must remain a matter of speculation.

This is particularly true of whooping-cough It was perhaps only natural, when acute encephalitis was recognized as a clinical entity following infectious diseases, that many of the nervous disorders of whooping-cough pointing to cerebral or spinal involvement should be ascribed to some similar inflammatory process.

When we consider the widespread prevalence of the disease and the high incidence of nervous complications—especially in the younger age-groups—we should expect to meet not a few cases showing the clear-cut clinical picture of encephalomyelitis, confirmed in a proportion of instances by the histological findings. Examination of the literature on this point, however, fails to reveal proof that encephalitic inflammation ever follows whooping-cough.

It has been observed that the attack of encephalitis is more dramatic and severe after measles, variola and vaccinia than after varicella, rubella, or mumps, while anti-rabic encephalitis occupies an intermediate position. *A priori*, one should expect pertussis encephalitis to be severe, with unequivocal changes. In a small personal series in which encephalitis was suspected as the cause of meningeal cerebral symptoms, acute congestion of the cerebral vessels was invariably found on autopsy, but there was no evidence of disseminated encephalomyelitis.

The question of ætiology is more than an academic one. The hypothesis which explains the occasional occurrence of encephalitis in the course of certain specific virus infections as due to the existence of dermatotropic and neurotropic properties in the same virus has much to commend it, but it must postulate some variation in

the soil as well as in the seed, for a given virus strain rarely produces more than a very occasional encephalitic complication.

If this hypothesis is the correct one, then the employment of immune measles or variolar serum in the treatment of post-measles or variolar encephalitis respectively, is a rational procedure from which a certain measure of success should reasonably be expected.

If, on the other hand, we accept the view that acute encephalitis is due to a specific virus, possibly widely disseminated in the country, and that the acute disease merely activates the specific virus or lowers the individual resistance to it, then we should expect little or no response to the therapeutic employment of measles or variola serum. Only immune encephalitis serum would possess the antibody we seek, and it would probably have equal therapeutic effect in measles, scarlet fever, or mumps. The numbers so treated have been too few and inadequately controlled to warrant any conclusion on the value of serum therapy. In any event, the more or less sudden onset and rapid evolution of the disease, going on to a fatal issue or to complete recovery, makes it doubtful whether immune serum will ever find much place in the treatment of the condition.

Dr. L. J. Laurent said he would like to bring forward some confirmation of Dr. Rolleston's remarks on diphtheritic paralysis.

There could be no doubt in the mind of anyone who had to treat diphtheria every day that the frequency and severity of diphtheritic paralysis bore a direct relationship to the severity of the initial toxæmia. When paralysis followed after comparatively mild attacks it had been his invariable experience that either the antitoxin had been given too late, or that it had been used in doses which were inadequate. Hemiplegia following diphtheria must be very rare; twelve years ago he saw two cases of it, but he had not encountered any since. In both those cases the patients had recovered, but were left with permanent spastic paralyses. Diphtheria toxin had a profound effect on the nervous system, especially on the autonomic nervous system. In confirmation of this, he had made certain observations on the oculo-cardiac reflex in cases of diphtheria, and in some cases it had been of small prognostic value. During the first three weeks of severe diphtheria one noted a remarkable exaggeration of this reflex, so that it was possible to stop the heart for a few seconds, or even to produce alarming symptoms of collapse; hence the reflex must be tried with great caution. In cases in which the reflex was absent in the presence of severe diphtheria, the prognosis was very grave, and usually there was a fatal issue. At a later stage of the disease, when there was no longer cause to dread circulatory failure, but in the presence of extensive paralysis, palatal and pharyngeal, the oculo-cardiac reflex might be normal or absent, or it might be reversed, i.e. pressure on the eyeballs produced an acceleration of the heart rate. In cases in which a slowing of the heart resulted, or in which there was scarcely any difference, the prognosis was good, the patients recovering in the usual way or fairly quickly. But when the oculo-cardiac reflex showed acceleration of the heart rate, the paralysis proved to be more serious, and the recovery of the patient was very slow.

With regard to paralysis of accommodation in diphtheria, he had never seen a case of diphtheria with loss of pupillary reflex to accommodation; it seemed to be entirely a paralysis of the ciliary muscle.

As to the serious complications of encephalitis and encephalomyelitis after acute infections, there was no doubt that these were very grave and important, and deserved all the work which had been done on them in regard to virus infections, but from the point of view of those who had to treat infectious diseases every day, these complications were found to play only a small part in the routine. The proportion of cases of encephalitis among patients with infectious fevers must be

very slight, and he was curious as to the number of cases of rubella in which any of these nervous manifestations developed.

With regard to whooping-cough, a matter which had not been mentioned was that frequently the convulsions following whooping-cough were due to tuberculous meningitis. Tuberculous meningitis and generalized tuberculosis occurred after whooping-cough more frequently than after any other infectious fever, even including measles; many times he had seen tubercle bacilli in the cerebrospinal fluid, proving the existence of tuberculous meningitis when it had not been previously suspected.

Ruling out cases of tuberculosis after whooping-cough, there occurred convulsions, the ætiology of which was obscure still. The convulsions of whooping-cough had been more or less associated, in his experience, with a condition of anoxæmia. The onset of these convulsions frequently coincided with the onset of bronchopneumonia, or with increased consolidation, or a sudden atelectasis of the lungs, and many of the convulsive attacks diminished in frequency and severity after the continuous administration of oxygen.

He hoped that the "endotoxin' isolated from the Bordet-Gengou bacillus, to which reference had been made, would prove a truly specific one, as this would eventually lead to the production of a specific antitoxin for the treatment of a very distressing condition.

Dr. E. Stolkind said that in his monograph "Paratyphoid Fever," and also in the *British Journal of Children's Diseases*, 1918, xv, 161, he had published several cases in which paratyphoid fever had been followed by nervous sequelæ—e.g. meningitis, meningeal symptoms, external hydrocephalus, epileptiform fits, psychoses, etc.

Dr. Russell Brain said that he found it equally difficult to accept the unitarian and the alternative theories as to the ætiology of the nervous complications of the exanthemata.

Dr. Wyllie had stressed one point which had always seemed to him (the speaker) important, namely, that though these disorders seemed to have a common pathological basis, there were certain distinctive features about them. Dr. Wyllie had mentioned some of them, such as differences in the mortality rates, and in the recovery rates, and others could be given. For example, in smallpox there was a tendency for curious speech disturbances or anarthria to develop; in chickenpox one noted the high percentage of patients with acute cerebellar ataxy, and the low mortality rate. In anti-rabic inoculation 35% of the cases developed acute ascending paralysis, which was very rare in the other conditions discussed, though it did occur as a rare manifestation of rabies infection itself in animals, and still more rarely in man.

Two alternatives had to be considered. If all these disorders were due to a common factor, that common factor must be modified, or directed in a surprising way against different parts of the nervous system, by the disorder acting as a predisposing cause. But if the primary virus was responsible for these complications it exhibited a curious and unexpected selectivity in its effects and in its mortality rates, as well as in its sequelæ. Thus both hypotheses carried with them difficulties. A good example of this was afforded by the unique case recorded by Knutti in the United States, in which a woman, ten days after vaccination, developed diffuse myelitis, with destruction of the grey matter and the white matter of the cord. Negri bodies were found in the ganglion cells in the nervous system, and experimental introduction of this into animals produced rabies.

He would like to mention the experimental work done on louping-ill, especially by Gordon and McLeod. Louping-ill produced a selective destruction of the Purkinje cells in the cerebellum, and it had been discovered by Gordon and McLeod that if

sheep were infected with the virus of that disease alone, they developed a generalized illness, but without nervous symptoms. For the nervous system to be implicated, it was necessary for the animals to be infected with another disease simultaneously, namely, tick-borne fever, and the same tick infected the animals at the same time with both the louping-ill and the tick-borne fever. Should that be confirmed, it would prove important in connexion with the subject of to-night's debate, as it was the first example on record of a virus being rendered neurotropic by a coincident infection with another virus.

He had been interested in Dr. Gunn's remarks, but he did not agree that serotherapy was necessarily going to afford a solution of the problem. If the nervous complications were due to the primary disease, one would expect it to respond to specific serotherapy, but if they were due to a secondary virus which was directed against the nervous system by the primary one and was so intimately related to it, one might expect that if the primary condition could be relieved by serotherapy, the other condition would subside. He had recently seen chickenpox encephalitis in a business man, aged 30, whose symptoms developed on the fourteenth day after infection. He exhibited mental confusion, weakness in one leg, and bilateral extensor responses. He made a good recovery and returned to work in a few weeks.

Dr. J. Purdon Martin said he had been trying to fit his own experience into the various classifications that had been given, and especially into Dr. Wyllie's classification. Most of the cases he had seen would fall into Dr. Wyllie's first group, in which lesions were apparently widespread in both cerebral hemispheres; he would refer to these later. Myelitic cases, which formed Dr. Wyllie's second group, he had seen only in adults, and then in association with influenza. The third group, the hemiplegic cases, he had seen also only in adults, and he recalled two instances in each of which one cerebral hemisphere was evidently very extensively affected, while there were practically no signs referable to the other hemisphere. Dr. Wyllie's fourth type, the ataxic type, he believed must be very rare; he could remember only one instance. Reverting to the first group—in which the symptoms were apparently due to damage in both cerebral hemispheres—he recalled three cases associated with measles, two that had occurred after vaccination, and two associated with food poisoning. (He had not been aware that this association had been recognized, but Dr. Wyllie evidently knew all about it.) He had also seen two similar cases in children in whom there was no indication of any exanthem or other acute general infection.

He had been much impressed by the mental symptoms in some cases. After convulsions had ceased the physical abnormalities might be relatively slight—the child was able to move all its limbs, the tendon-jerks did not show much change and the plantar reflexes were indefinite or only weakly extensor—but the mental symptoms might be very severe. When the convulsions had ceased the child appeared to have complete amentia. It gave not the slightest sign of intelligence and showed no appreciation of what was going on around it. Except that it breathed and had a temperature of 98·4° F. it might be a log of wood. After a few days it began to whine, and this whining (which he had seen in at least three cases) went on continuously thereafter, every moment that the child was awake. After several days, or perhaps a week, there came a day when the whining ceased whenever the nurse attended to the child or even stood at the bedside. This was the first indication of any contact of the child's nervous system with the environment. After this the whining gradually came to an end. One of his patients at this stage had shown very marked automatic groping and grasping movements, but this did not indicate any conscious appreciation of what was touched or grasped. In the next stage the child began to move its eyes, and it was apparent that it was taking some

notice. Hitherto it had been very difficult to know whether the child actually saw, and similarly whether it heard and, in some cases at any rate, he was sure that there was no conscious sight or hearing in the earlier stages. Gradually the child became more easy to feed and began to understand what was required of it. As its intelligence returned during the next few weeks, it passed quickly through the stages through which a baby passes more slowly. It became possible to get its attention —at first very briefly, afterwards for more prolonged periods—then to obtain simple answers from it, and after that the return of intelligence was rapid, although sometimes even after many weeks one might have the fear that the child was going to be an imbecile for the rest of its life. In two of his cases speech had been the last thing to recover. In one of these instances the child seemed to have recovered full intelligence, behaved normally, understood all that was said to her and played with the other children in the ward but she could not speak, and speech did not return until after she had left hospital. In the other instance the return of speech was not so long delayed and in both cases recovery was complete.

As regards the outlook: In one of his vaccination cases the patient had died, but in the other vaccination case and in all the rest of the cases the patients had made complete recoveries. He was surprised at the high figure of residual disabilities in measles cases which Dr. Wyllie had quoted. In the few cases that he (the speaker) had seen recovery had been complete. In one of them it had taken much longer than in the other two. Dr. Wyllie had mentioned that there were two different varieties of encephalitis which might occur in measles; the more usual one, the demyelinating type, came on after the seventh day or so, the other, the toxic type, came on before the rash came out. In the case to which he (the speaker) referred the child went into convulsions and became comatose before the rash appeared. After three months although she had made considerable recovery she was still an imbecile and had a stolid appearance with a certain degree of Parkinsonism. He learned afterwards, however, that recovery had eventually been complete and that the child had since been getting on well at school. From this case and from the food-poisoning cases which he had seen, he wondered whether the toxic cases were perhaps more severe and longer in their course than those of the demyelinating type.